VOLUME 79 • FEBRUARY 1959 • NUMBER 2

ARCHIVES OF DERMATOLOGY

Keratoacanthoma
R. H. Rigdon

Methoxsalen and Sun-Tanning
Otto C. Stegmaier

Relaxin (Releasin) Therapy in Diffuse Progressive Scleroderma
James A. Evans

Observations on Radiation Exposure in Dermatologic X-Ray Therapy
Herbert S. Alden, H. Stephen Weens, and Harry D. Youmans

Clinical Evaluation of Antipruritic Drugs
Frank E. Cormia and John W. Dougherty

Changes in the Ten Commonest Dermatoses in Private Practice
Edward F. Corson, Herbert A. Luscombe, and Joseph K. Corson

Chromoblastomycosis Treated with Local Infiltration of Amphotericin B Solution
Maurice J. Costello, Charles P. DeFeo Jr., and M. L. Littman

Pseudohypoparathyroidism
Carl W. Laymon and Alvin Zelickson

Erythema Elevatum Diutinum
Warren L. Macaulay

Laboratory Studies in a Series of Biologic False-Positive Reactors
J. Lowry Miller, Marvin Brodey, and Justina H. Hill

The Education of the Dermatologist in the Soviet Union
Maximilian E. Obermayer

On Sudden or Rapid Whitening of the Hair
Alfred J. Ephraim

Methoxsalen in the Treatment of Vitiligo
Joseph A. Elliott Jr.

Skin-Marking Technique
John van de Erve

The New, Newer, and Newest

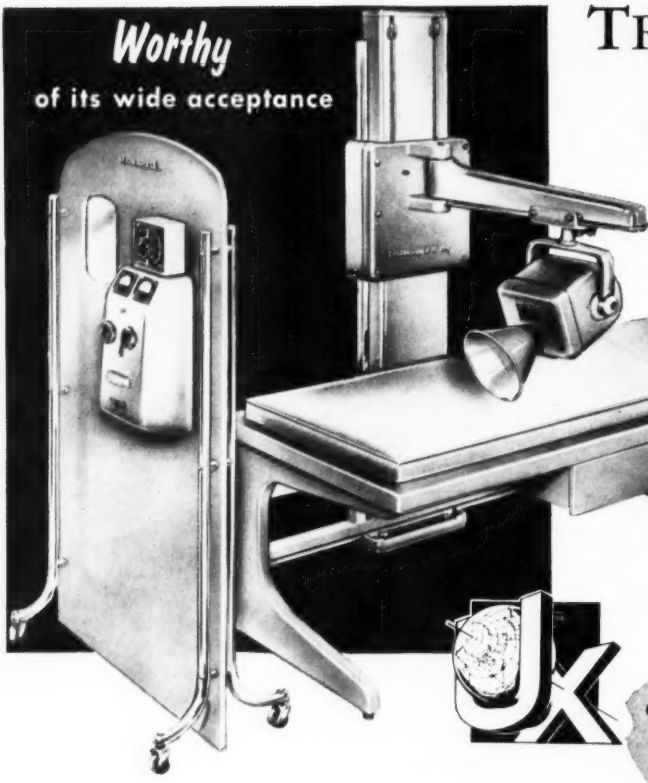
Correspondence

Los Angeles Dermatological Society

New York Dermatological Society

Announcements

AMERICAN MEDICAL ASSOCIATION PUBLICATION

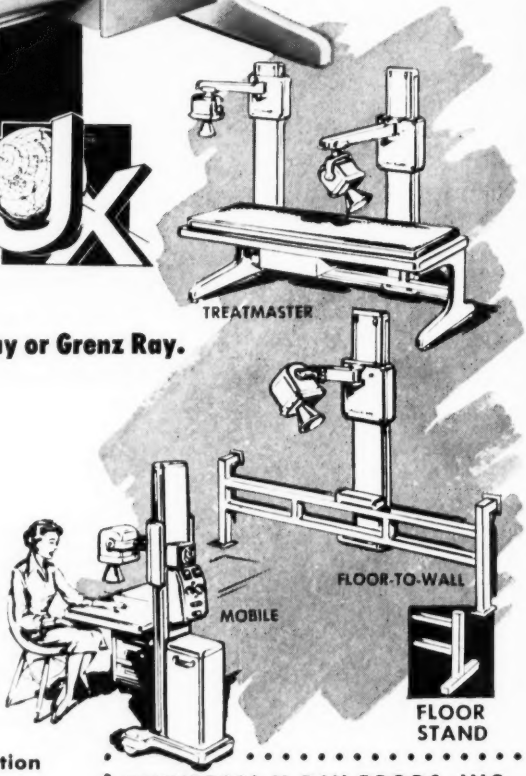


TREATMASTER

GRENZ RAY THERAPY UNITS

by UNIVERSAL

Manufacturers of fine equipment for over 30 years



A wide variety of models in either X-Ray or Grenz Ray.

Universal skin therapy X-Ray and Grenz Ray units are available in a variety of models to suit most any type of office layout. Any model you choose has the same high standards of craftsmanship and unique advantages that has made the Universal skin therapy line so outstanding among the many leading dermatologists, hospitals and clinics throughout the world.

- **High output—desirable quality of radiation**
- **Simple and convenient handling**
- **Safety in everything from lead shielding to electrical and mechanical construction**
- **Priced within the reach of even the doctor just starting practice**

You owe it to yourself to investigate

SEND NOW FOR FREE TECHNICAL DATA

UNIVERSAL X-RAY PRODS. INC.

1140 N. Western Ave. • Chicago 22, Ill. • U. S. A.

Please mail more detailed prices and information on:

☐ X-Ray Therapy ☐ Grenz Ray Therapy

Doctor_____

Address _____

City_____ State_____

TABLE OF CONTENTS

VOLUME 79 FEBRUARY 1959 NUMBER 2

ORIGINAL ARTICLES

PAGE

Keratoacanthoma
R. H. Rigdon, M.D., Galveston, Texas 139

Methoxsalen and Sun-Tanning
Otto C. Stegmaier, M.D., Davenport, Iowa 148

Relaxin (Releasin) Therapy in Diffuse Progressive Scleroderma
James A. Evans, M.D., Boston 150

Observations on Radiation Exposure in Dermatologic X-Ray Therapy
Herbert S. Alden, M.D.; H. Stephen Weens, M.D., and Harry D. Youmans, B.S., Atlanta 159

Clinical Evaluation of Antipruritic Drugs
Frank E. Cormia, M.D., and John W. Dougherty, M.D., New York 172

Changes in the Ten Commonest Dermatoses in Private Practice
Edward F. Corson, M.D.; Herbert A. Luscombe, M.D., and Joseph K. Corson, M.D., Philadelphia 179

Chromoblastomycosis Treated with Local Infiltration of Amphotericin B Solution
Maurice J. Costello, M.D.; Charles P. DeFeo Jr., M.D., and M. L. Littman, M.D., Ph.D, New York 184

Pseudohypoparathyroidism
Carl W. Laymon, M.D., and Alvin Zelickson, M.D., Minneapolis 194

Erythema Elevatum Diutinum
Warren L. Macaulay, M.D., Fargo, N. D. 202

Laboratory Studies in a Series of Biologic False-Positive Reactors
J. Lowry Miller, M.D.; Marvin Brodey, M.D., and Justina H. Hill, D.Sc., New York 206

The Education of the Dermatologist in the Soviet Union
Maximilian E. Obermayer, M.D., Los Angeles 213

On Sudden or Rapid Whitening of the Hair
Alfred J. Ephraim, M.D., Brooklyn 228

Methoxsalen in the Treatment of Vitiligo
Joseph A. Elliott Jr., M.D., Charlotte, N. C. 237

CLINICAL NOTES, NEW INSTRUMENTS AND TECHNIQUES

Skin-Marking Technique
John van de Erve, M.D., Charleston, S. C. 244

The New, Newer, and Newest 245

CORRESPONDENCE

Education of the Dermatologist in Russia
M. E. Obermayer, M.D., Los Angeles 226

Larva Currens
G. H. N. Clarke, M.D., Lagos, Nigeria, West Africa 247

SOCIETY TRANSACTIONS

Los Angeles Dermatological Society 248
New York Dermatological Society 251

REGULAR DEPARTMENTS

Announcements 258

A. M. A.
ARCHIVES OF DERMATOLOGY

VOLUME 79 FEBRUARY 1959 NUMBER 2

COPYRIGHT, 1959, BY THE AMERICAN MEDICAL ASSOCIATION

EDITORIAL BOARD

HERBERT RATTNER, Chief Editor

104 South Michigan Avenue, Chicago 3

HARVEY BLANK, Miami, Fla.

LOUIS BRUNSTING, Rochester, Minn.

J. LAMAR CALLAWAY, Durham, N. C.

A. C. CIPOLLARO, New York

GEORGE M. LEWIS, New York

H. E. MICHELSON, Minneapolis

J. F. HAMMOND, Editor, A. M. A. Scientific Publications

GILBERT S. COOPER, Managing Editor, Specialty Journals

SUBSCRIPTION RATES

Price per annum in advance, including postage: Domestic, $12.00. Canadian, $12.50. Foreign, $13.50. Price to students, interns, and residents, $7.00 in U. S. & possessions.

Single copies of this and previous calendar year, $1.25.

Back issues older than two years are available through Walter J. Johnson, Inc., 111 Fifth Avenue, New York 3. Future reprints of back issues will be available through Johnson Reprint Corporation, 111 Fifth Avenue, New York 3.

Checks, money orders, and drafts should be made payable to the American Medical Association, 535 North Dearborn Street, Chicago 10.

AMERICAN MEDICAL ASSOCIATION Publication

Published monthly by the AMERICAN MEDICAL ASSOCIATION. Editorial and Circulation Offices: 535 North Dearborn Street, Chicago 10, Illinois. Publication Office: Thompson Lane, Box 539, Nashville 1, Tennessee.

Second-class postage paid in Nashville, Tennessee.

CHANGE OF ADDRESS: When there is a change of address, the Circulation Office of the American Medical Association should be notified at least six weeks before the change is made. The address label clipped from the subscriber's latest copy of the publication and a statement of old and new address should be included. If there is a postal zone number, it too should be included in the new address. The instructions should state whether the change is permanent or temporary.

When your patient suffers from histamine-induced skin reaction

Whether caused by drugs, dander, or detergents, histamine-induced skin reactions (such as the sulfonamide reaction shown above) respond rapidly to 'Teldrin' *Spansule* capsule therapy.

Just one capsule in the morning, another at night, provides 24-hour antihistamine effect. And because of the prolonged, even release of 'Teldrin' medication, side effects are minimal.

Teldrin* Spansule*

chlorprophenpyridamine maleate — sustained release capsules, S.K.F.

Smith Kline & French Laboratories, Philadelphia

*T.M. Reg. U.S. Pat. Off.

Instructions to Contributors

Articles, book reviews, and other materials for publication should be addressed to the Chief Editor. Articles are accepted for publication on condition that they are contributed solely to this journal.

An original typescript of an article, with one carbon copy, should be provided; it must be double or triple spaced on one side of a standard size page, with at least a 1-inch margin at each edge. Another carbon copy should be retained by the author.

The main title of an article may not contain more than eighty characters and spaces; a subtitle may be of any length.

The author's name should be accompanied by the highest earned academic or medical degree which he holds. If academic connections are given for one author of an article, such connections must be given for all other authors of the article who have such connections.

If it is necessary to publish a recognizable photograph of a person, the author should notify the publisher that permission to publish has been obtained from the subject himself if an adult, or from the parents or guardian if a child. An illustration that has been published in another publication should be accompanied by a statement that permission for reproduction has been obtained from the author and the original publisher.

Oversized original illustrations should be photographed and a print on glossy paper submitted. Prints of a bluish tinge should be avoided. Large photomicrograph prints will be reduced in scale unless portions to be cropped are indicated by the author. The author should submit duplicate prints of roentgenograms and photomicrographs with the essential parts that are to be emphasized circled, as a guide to the photoengraver.

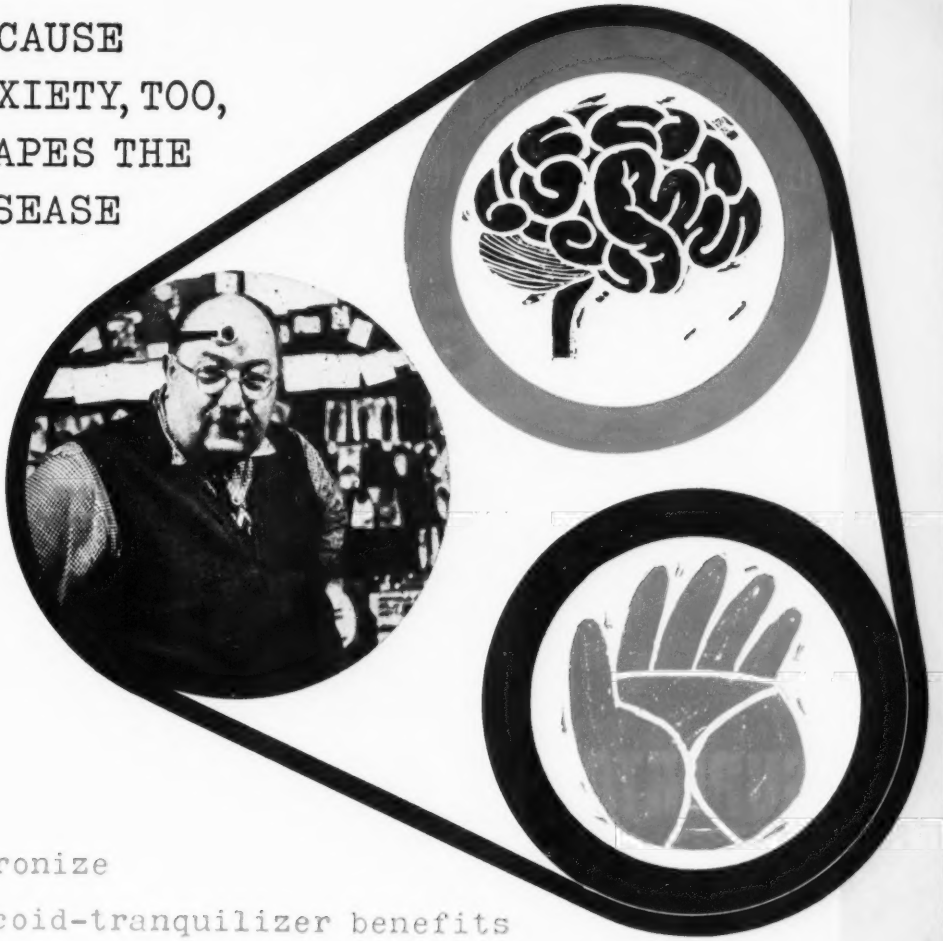
Charts and drawings should be in black ink on hard, white paper. Lettering should be large enough, uniform, and sharp enough to permit necessary reduction. Glossy prints of x-rays are requested. Paper clips should not be used on prints, since their mark shows in reproduction, as does writing on the back of prints with hard lead pencil or stiff pen. Labels should be prepared and pasted to the back of each illustration showing its number, the author's name, and an abbreviated title of the article, and plainly indicating the top. Charts and illustrations must have descriptive legends, grouped on a separate sheet. Tables must have captions. ILLUSTRATIONS SHOULD BE UNMOUNTED.

References to the literature should be limited to those used by the author in preparation of the article. They should be typed on a special page at the end of the manuscript. The citation should include, in the order given, name of author, title of article (with subtitle), name of periodical, with volume, page, month—day of month if weekly or biweekly—and year. References to books must contain, in the order given, name of author, title of book, city of publication, name of publisher, and year of publication.

AMERICAN MEDICAL ASSOCIATION

535 North Dearborn Street **Chicago 10**

BECAUSE
ANXIETY, TOO,
SHAPES THE
DISEASE



synchronize

corticoid-tranquilizer benefits

in steroid-responsive dermatoses

STEROTRIL*

METICORTEN and TRILAFON

Schering

improves outward eruption • promotes healing and clearing of lesions • helps relieve intense pruritus • provides antiallergic, anti-inflammatory benefits

modifies inward disruption • relaxes tension that "lashes" itch • stops scratching that adds itch-insomnia to injury in neurodermatitis, atopic dermatitis, exfoliative dermatitis and all dermatologic allergies aggravated by inner turmoil

STEROTRIL Tablets, 2.5 mg. METICORTEN® (prednisone) and 2 mg. TRILAFON® (perphenazine); bottles of 30 and 100.

SCHERING CORPORATION • BLOOMFIELD, NEW JERSEY

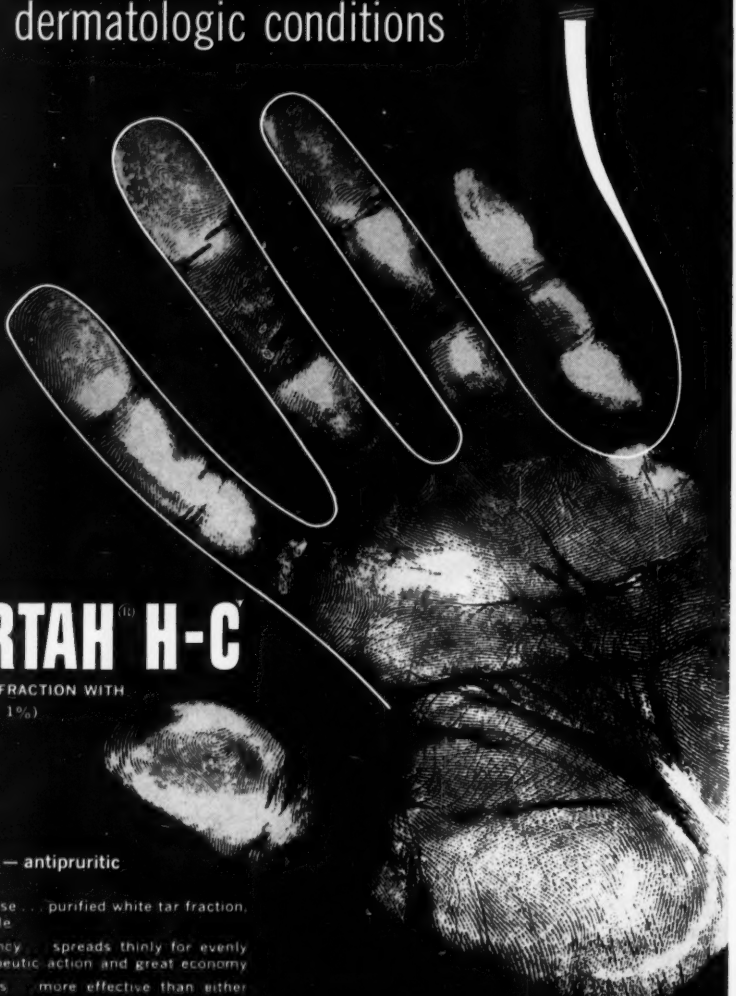
*T.M.

ST-J-319

spreads

THINLY · EVENLY · ECONOMICALLY

in acute dermatologic conditions



SUPERTAH® H-C

(1.25% COAL TAR FRACTION WITH HYDROCORTISONE 1%)

antiinflammatory — antipruritic

- water miscible base . . . purified white tar fraction, stainless, washable
- maximum efficiency . . . spreads thinly for evenly distributed therapeutic action and great economy
- enhanced benefits . . . more effective than either agent alone
- excellent response . . . deep penetration to source of inflammation

supplied: ½-oz. tube

also available

SUPERTAH Ointment (1½-oz. tube)
provides the therapeutic effectiveness of time proved tar medication

SUPERTAH S/S (with salicylic acid and sulfur; 1½-oz. tube)
for keratolytic action

All Supertah preparations are made with refined natural coal tar fraction

TAILBY-NASON COMPANY, INC. DOVER, DELAWARE

stop penicillin reactions

before they become serious

NEUTRAPEN®

(NEUTRAlizes PENicillin) (Penicillinase Injectable,* SchenLabs)

the only specific for penicillin reactions

"... if every patient with a penicillin reaction were given penicillinase [NEUTRAPEN] *within 24 to 48 hours ... I do not think we would see the severe, prolonged reactions we are seeing now."*

R. M. Becker, Antibiotics Annual 1957-58.[1]

Unlike the antihistamines, ACTH or steroids which treat effects, NEUTRAPEN, an enzyme, aborts penicillin reactions by counteracting their cause—it destroys the penicillin itself and is effective in about 97 per cent of cases.[2] Over 80 per cent of patients obtain clearing of the reaction with one injection.[3]

Obscure sources—even cases with no history of penicillin therapy respond to NEUTRAPEN when the reaction has been caused by penicillin from such sources as milk, Roquefort or bleu cheese, or penicillin containing vaccines.[3]

NEUTRAPEN—800,000 units I.M.—should be given as soon as symptoms appear. May be repeated on the third day if response is not satisfactory. In anaphylactic reactions, after routine emergency measures—800,000 units intravenously, followed immediately by 800,000 units intramuscularly.
contraindications: None. *side effects:* Occasionally transient local soreness, erythema, and edema; rarely, transitory chills and fever.
supplied: 800,000-unit single-dose vials of lyophilized penicillinase powder. Stable at room temperature in the dry state.
references: (1) Becker, R. M., in Welch, H., and Marti-Ibañez, F.: Antibiotics Annual 1957-1958, New York, Medical Encyclopedia, Inc., 1958, p. 310. (2) Zimmerman, M. C.: Clin. Med. *5*:305, 1958. (3) Zimmerman, M. C.: J.A.M.A. *167*:1807, 1958.

®T. M. REG. U. S. PAT. OFF. *PATENTS PENDING. 55658

SchenLabs SCHENLABS PHARMACEUTICALS, INC • NEW YORK 1, N. Y.

In Acne

TUCKS®

soft cotton flannel pads saturated with witch hazel (50%) and glycerine (10%). pH about 4.6

answers a dermatologic and an emotional need

Cleansing, solvent, mildly astringent TUCKS provides a new and valuable therapeutic aid for the treatment of acne.

At home in their handy jars, or *at school* in the moisture-tight plastic envelope provided, soothing Tucks pads promote the thorough skin care indispensable to the successful treatment of acne.

Always ready for use, TUCKS encourages cleanliness when used as finger shields for expressing comedones.

fuller PHARMACEUTICAL COMPANY
Minneapolis 16, Minn.

For a generous office supply of TUCKS —just fill in and return this card.

Name_____

Address_____

City_____ Zone____ State_____

integrate your knowledge by reading these related specialty journals . . .

A. M. A. Archives of INDUSTRIAL HEALTH

A. M. A. Archives of INTERNAL MEDICINE

A. M. A. Archives of DERMATOLOGY

Designed to save you hours of reading time through visual presentations . . . to provide you with timely tips every month . . . to place useful information at your finger tips, leaving less information on your reference shelf.

Write for subscriptions to:
AMERICAN MEDICAL ASSOCIATION
535 North Dearborn Street
Chicago 10, Ill.
Dept. (PATH.)

For the treatment of dry, scaly skin

LOWILA®
EMOLLIENT

an effective skin moisturizer

moisturizes and softens the skin

promotes moisture retention

supplements natural skin oils

restores and maintains normal skin pH

Lowila Emollient hydrates the skin . . . keeps it soft and smooth

Lowila Emollient is a new, effective skin moisturizer for the treatment of dry, scaly skin. It contains an excellent keratin-moisturizing agent Kerohydric®, a crystal-clear, dewaxed oil-soluble fraction derived from lanolin.

Lowila Emollient moisturizes the skin and promotes retention of moisture. When applied to the skin, Lowila Emollient provides a partially-occlusive "breathing" film that: (1) supplies its own water to the dehydrated keratin layer, (2) prevents excessive evaporation when the atmosphere is dry, (3) allows the skin to absorb water from an atmosphere with normal humidity.

Lowila Emollient also supplements natural skin oils, restoring the protective action of skin lipids lost through effects of water, weather and detergents. In Lowila Emollient, Kerohydric is dispersed in a lactic acid buffered emulsion that restores and maintains normal skin acidity.

LOWILA EMOLLIENT

Indications

For dryness, flaking and scaling following therapy of acute inflammation
Dermatitis of the hands ("Housewives' eczema")
In chronic atopic dermatitis
Pruritus senilis—pruritus hiemalis
In nummular dermatitis
In psoriasis
Xerosis or asteatosis
Sunburn
Diaper rash
Chafed or chapped skin
Ichthyosis

Caution: Lowila Emollient is partially occlusive. Therefore it should not be used until the skin is free of inflammation.

Application:

Gently rub a small amount into affected areas three or more times a day and at bedtime. Use particularly after exposure to water, soap and detergents.

Availability:

Lowila Emollient is supplied in 62.5 gram tubes.

WESTWOOD PHARMACEUTICALS
Division of Foster-Milburn Company
Buffalo 13, New York

CONTROL EMOTIONAL FLARE-UPS

that cause or aggravate SKIN ERUPTIONS

Miltown®

meprobamate (Wallace)

In neurodermatitis, atopic dermatitis, chronic urticaria, eczematoid dermatitis, lichen planus, psoriasis, pruritus ani, pruritus vulvae

Eighty per cent of 224 patients with a wide variety of skin disorders responded favorably to adjunctive therapy with Miltown.[2]

"is an effective addition to conventional dermatological therapy."[1]

- relieves anxiety and tension with exceptional safety
- suitable for prolonged administration
- does not impair physical efficiency or mental alertness

References: 1. Sokoloff, O. J.: Meprobamate (Miltown) as adjunct in treatment of anogenital pruritus. A.M.A. Arch. Dermat. **74**:393, Oct. 1956. 2. LeVan, P.: Clinical dermatologic studies of four chemically different tranquilizers. Clinical Med. **4**:1089, Sept. 1957.

Literature and samples on request

WALLACE LABORATORIES, *New Brunswick, N. J.*

CM-7260

you
can prescribe for
more
patients
with inflammatory and allergic dermatoses

unsurpassed therapy...
with
great security...

Aristocort®

Triamcinolone LEDERLE

Several hundred patients with inflammatory and allergic dermatoses (including *psoriasis, atopic dermatitis, exfoliative dermatitis, pemphigus, dermatitis herpetiformis, eczematoid dermatitis, contact dermatitis* and *angioneurotic edema*) have been treated with ARISTOCORT for substantial periods up to one year. Good to excellent results have been achieved with dosages of ARISTOCORT averaging ⅓ to ½ those of previous corticosteroids.

Highly successful results were obtained by Hollander and his group[1] and Shelley and associates[2] in the treatment of psoriasis with ARISTOCORT. The former found that when ARISTOCORT was temporarily replaced by prednisolone in 9 patients, there was prompt recurrence of psoriasis, which again disappeared on resumption of ARISTOCORT. Side effects usually were of "mild degree and detracted little from the delight of most of the patients in their improved skin condition."

Shelley and associates found it "gratifying to have a steroid compound which did not lead to fluid retention and edema." They reported that 4 mg. of ARISTOCORT were equivalent in efficacy to 10 mg. of prednisolone in treating dermatites.

Rein and associates[3] reported on patients with severe dermatitis who were treated with ARISTOCORT. Most of these patients had previously been on prednisolone. ARISTOCORT controlled the symptoms effectively on ⅔ the dosage of prednisolone. There was only a low incidence of side effects that did not require interruption of therapy.

Appel and associates[4] and Friedlaender and Friedlaender[5] have also found ARISTOCORT effective in treating dermatoses with about ½ to ⅔ the dosages required with prednisone and prednisolone. The former group found that with ARISTOCORT there were no psychiatric disturbances, no hypertensive changes in any of the patients, and no abnormalities of electrolytes.

Supplied: 1 mg. scored tablets (yellow); 2 mg. scored tablets (pink); 4 mg. scored tablets (white).

Bibliography:

1. *Hollander, J. L.; Brown, E. M., Jr.; Jessar, R. A.; Smukler, N. M.; Udell, L.; Stevenson, C. R., and Bowie, M. A.: Paper read before Interim Session, American Rheumatism Association, Bethesda, Maryland, Dec. 6, 1957.*
2. *Shelley, W. B.; Harun, J. S., and Pillsbury, D. M.:* J.A.M.A. *167:959, 1958.*
3. *Rein, C. R.; Fleischmajer, R., and Rosenthal, A. L.:* J.A.M.A. *165:1821, 1957.*
4. *Appel, B.; Tye, M. J., and Leibsohn, E.: Antibiotic Med. & Clin. Ther. 5:716 (Dec.) 1958.*
5. *Friedlaender, S., and Friedlaender, A. S.: Antibiotic Med. & Clin. Ther. 5:315, 1958.*

Lederle

LEDERLE LABORATORIES, A Division of AMERICAN CYANAMID COMPANY, Pearl River, N.Y.

NEW
TOPICAL
DIMENSIONS
in

Antiinflammatory
Antipruritic
Antiallergic
Bactericidal
Fungicidal
Protozoacidal
} action

INCORPORATED IN EXCLUSIVE ACID MANTLE® VEHICLE

pH 5.0
Creme
COR-TAR-QUIN™

ACID MANTLE® · hydrocortisone · stainless tar · diiodohydroxyquinoline

In subacute and chronic dermatoses, "especially where an inflammatory reaction was accompanied by increased scaling and lichenification with secondary infection such as is seen in seborrheic dermatitis, atopic dermatitis, contact dermatitis, and neurodermatitis."

—Rein, C. R., and Fleischmajer, R.: Personal Communication.

also available COR-TAR-QUIN LOTION

Sig: Apply b. i. d.
½ oz., 1 oz., 2 oz., & 4 oz. tubes
either 0.5% or 1.0% hydrocortisone.

DOME Chemicals Inc.
109 WEST 64 ST., NEW YORK 23, N.Y.
In Canada: 2765 Bates Rd., Montreal, P.Q.

athlete's foot

it's a family problem...

except for me

Athlete's Foot—one of the most prevalent and troublesome fungus infections today — is estimated to affect 90% of the population at one time or another. Desenex, containing the unsaturated fatty acid, undecylenic acid, has proved to be one of the most potent antimycotic agents known for effective treatment of superficial fungus infections.

Night and Day Treatment

At Night — Desenex Ointment (zincundecate) — 1 oz. tubes. **During the Day** — Desenex Powder (zincundecate) — 1½ oz. container. Also — Desenex Solution (undecylenic acid) — 2 fl. oz. bottles. In Otomycosis — Desenex Solution or Ointment.

Maltbie **Write for samples**

MALTBIE LABORATORIES DIVISION
Wallace & Tiernan Inc. • Belleville 9, N. J.

Desenex®
FOR ATHLETE'S FOOT

fast relief from itching
prompt antimycotic action
continuing prophylaxis

PD-91

ACCUMULATING EVIDENCE shows the

CLINICAL STUDY OF CADMIUM SULFIDE SHAMPOO

Canad. M. A. J. *79*:917 (Dec. 1) 1958

"In treatment of seborrhoea of the scalp with cadmium sulfide 1% (Capsebon), a good result was obtained in 71% of the 127 cases, a fair result . . . in 15%, and no result in 14%. The preparation is an excellent shampoo. Its use does not bring about 'rebound' oiliness. No toxic side effects were seen."

J. H. HARVEY, M.D., and L. P. EREAUX, M.D.

PRELIMINARY AND SHORT REPORT

CADMIUM SULFIDE SHAMPOO IN SEBORRHEA CAPITIS

J. Invest. Dermat. *29*:159 (Sept.) 1957

"Of eighty-four patients treated for seborrheic problems in the scalp with . . . cadmium sulfide shampoo . . . seventy-nine [94%] obtained good to excellent results."

W. L. KIRBY, M.D.

New Beneficial Agents in the Treatment of Acne Vulgaris and Seborrheic Dermatitis

Postgrad. Med. *24*:439 (Oct.) 1958

" . . . this preparation does appear to be one of the better antiseborrheic agents. The effectiveness and cosmetic acceptability of this preparation would appear to warrant its further use."

D. G. STOUGH, M.D.; ROBERT LEWIS, M.D.; B. L. FARMER, M.D.; L. S. OSMENT, M.D., and R. O. NOOJIN, M.D.

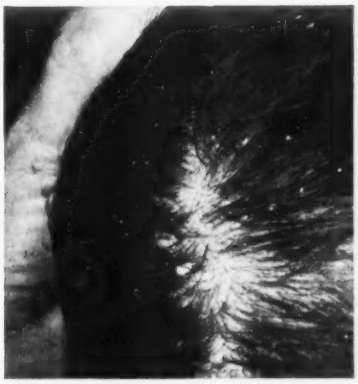
Cadmium Shampoo Treatment Of Seborrheic Dermatitis

Texas J. Med. *53*:640 (Aug.) 1957

" . . . an extremely useful agent in control of chronic or recurrent seborrhea of the scalp . . . an important contribution . . . "

J. FRED MULLINS, M.D., and JAMES R. BARNETT, M.D.

effectiveness of this therapeutic shampoo



BEFORE

AFTER

THESE STATEMENTS REFLECT THE GROWING RECOGNITION OF CAPSEBON'S

- effectiveness
- high degree of safety
- cosmetic acceptability

Capsebon is easy to apply—easy as an ordinary shampoo, and just as quick.

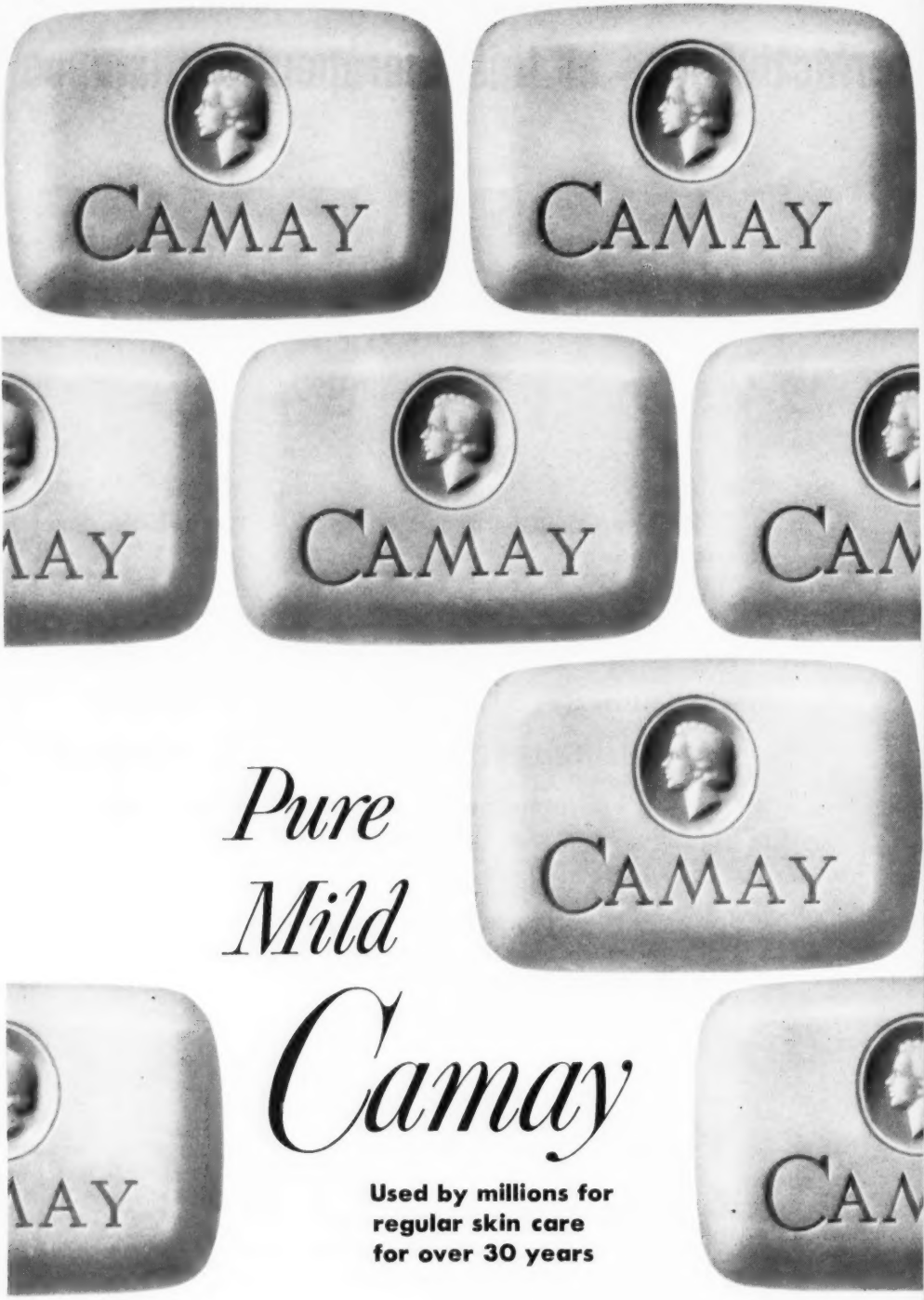
Available in 4-oz. bottle, on prescription only.

Additional references available from Professional Service Department on request.

Capsebon™

1% cadmium sulfide suspension

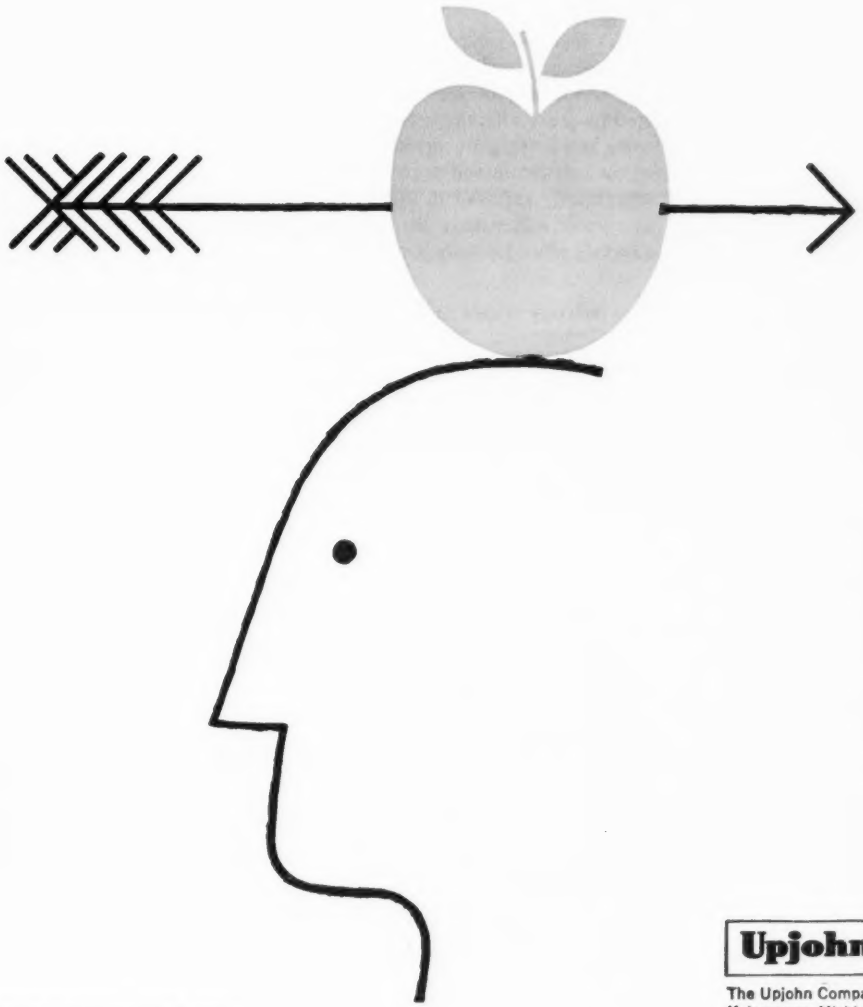
PITMAN-MOORE COMPANY
DIVISION OF ALLIED LABORATORIES, INC.
INDIANAPOLIS 6, INDIANA



©P&G Procter & Gamble

Medrol*

hits the disease but spares the patient



*TRADEMARK FOR METHYLPREDNISOLONE, UPJOHN

Upjohn

The Upjohn Company
Kalamazoo, Michigan

announcing

a new topically superior

now available

for topical application in dermatotherapy

Kenalog (triamcinolone acetonide) is a new synthetic corticoid compound with powerful anti-inflammatory and antipruritic action. Developed by the Squibb Institute for Medical Research, and evaluated during preliminary clinical trials in over 1,000 patients, Kenalog used topically has demonstrated its great effectiveness in controlling most common dermatoses.[1] Symptoms of itching and burning are dramatically relieved after topical application of Kenalog.[1,2] A superior agent for both acute and chronic dermatoses, its unexcelled anti-inflammatory action is most clearly apparent in the treatment of chronic, therapeutically refractory conditions, such as chronic eczematous dermatitis.[3] Complete resolution is often obtained with Kenalog where certain other topically applied steroids have failed.[3]

Kenalog in ointment, cream or lotion form may be used for treatment of a wide variety of dermatoses including:

Atopic dermatitis
Contact dermatitis
Eczematous dermatitis
Neurodermatitis
Seborrheic dermatitis
Insect bites
Pruritus ani
Pruritus vulvae
Lichen simplex chronicus
Exfoliative dermatitis
Stasis dermatitis
Nummular eczema

Kena

SQUIBB

Squibb Quality – the Priceless Ingredient

nti-inflammatory steroid

Kenalog effectively provides for prompt symptomatic relief as well as control of many common dermatologic disorders.[1-7]

In double-blind tests in 309 patients comparing 0.1% Kenalog and 1.0% hydrocortisone, Kenalog exhibited superior anti-inflammatory, antiallergic and antipruritic activity.

Investigator	Total Cases	Kenalog Superior	Hydrocortisone Superior	Neither Effective	Equally Effective
Goodman[3]	50	32	3		15
Smith et al.[4]	109	75	3	3	28
Fitzpatrick et al.[5]	120	61	5		54
Lerner[6]	30	20	4	1	5
	309	188	15	4	102

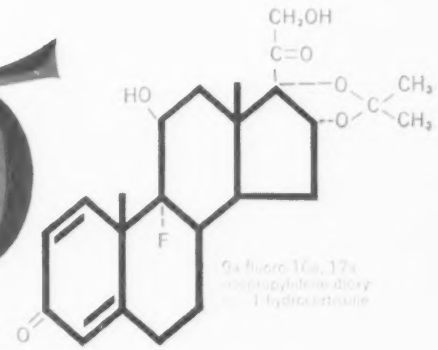
Kenalog is extremely well tolerated locally. No systemic toxicity has been observed in clinical studies, published and in progress, involving over 1,000 patients.[1,3] Metabolic studies show that there is no electrolyte disturbance when Kenalog is applied topically.[1,4,5]

1. Reports to the Squibb Institute for Medical Research.
2. Howell, C. M.: Squibb Clinical Research Notes 1:5 (Oct.) 1958.
3. Goodman, J. J.: Ibid. p. 1.
4. Smith, J. G.; Zawisza, R. J., and Blank, H.: Ibid. p. 6.
5. Fitzpatrick, T.; Crowe, F. W., and Walker, S. A.: Ibid. p. 12.
6. Lerner, A. B.: Ibid. p. 2.
7. Robinson, R. C. V.: Bull. School of Med., U. Maryland 43:54 (July) 1958.

Supply
Kenalog cream, 0.1% – 5 Gm. and 15 Gm. tubes.
Kenalog lotion, 0.1% – 15 cc. plastic squeeze bottles.
Kenalog ointment, 0.1% – 5 Gm. and 15 Gm. tubes.

log

Triamcinolone Acetonide



"KENALOG" IS A SQUIBB TRADEMARK

DERMPAK

Therapeutic Gloves

For a time-saving and convenient method of wet compress therapy dermatologists are turning to DERMPAK Therapeutic Gloves when treating eczematous processes of the hands.

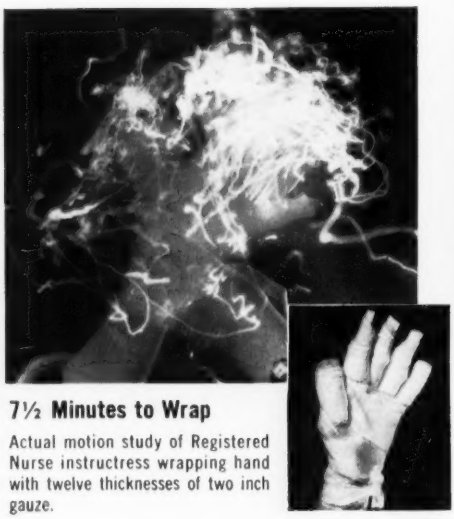
DERMPAK Gloves are widely accepted because they not only conserve valuable personnel time but meet with exceptional acceptance by the patient.

DERMPAK Gloves are made of 12-ply quilted hospital gauze . . . sterilized before packaging. They are durable and may be washed and re-used many times.

Available, one pair to a sealed package, in small, medium or large sizes.

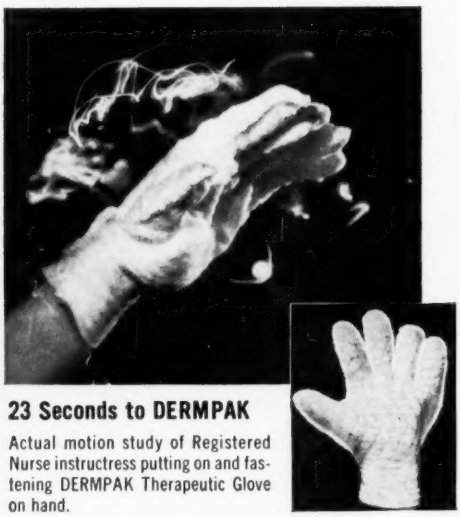
A free sample glove will be sent on request.

save
time
and
motion
where
wet packs
are
required...



7½ Minutes to Wrap

Actual motion study of Registered Nurse instructress wrapping hand with twelve thicknesses of two inch gauze.

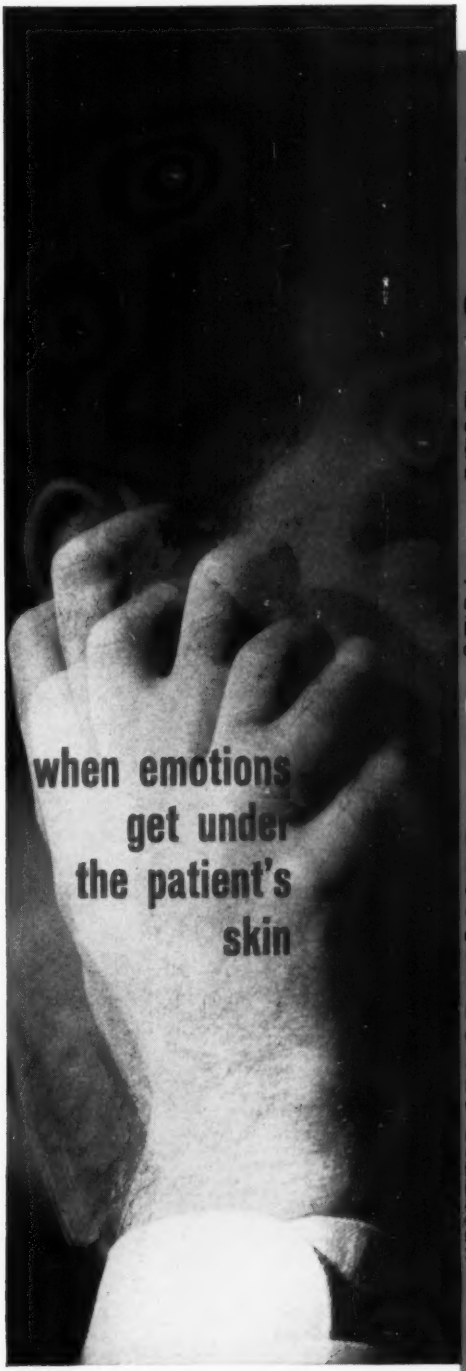


23 Seconds to DERMPAK

Actual motion study of Registered Nurse instructress putting on and fastening DERMPAK Therapeutic Glove on hand.

DERMPAK CORPORATION
282 East 5th Street • St. Paul, Minnesota

Manufactured and distributed under license from the Minnesota Dermatological Society.



A TRANQUILIZER UNIQUE
IN DERMATOLOGIC PRACTICE

dermatoses respond to the calming action

Feinberg: "Tranquilizing drugs in general have an equivocal effect on the manifestations of allergic disease. . . . ATARAX may be one exception to the rule. . . ."[1]

and the anti-allergic effect

—Added antihistaminic action of ATARAX controls a wide variety of dermatological exacerbations: pruritus, urticaria, dermatitis, and other cutaneous eruptions.[2,3,4,5]

# of ATARAX®

(brand of hydroxyzine)

Feinberg[1] obtained "most striking results" in 17 patients with chronic urticaria. The effect of ATARAX was excellent in 15, fair to good in 2. After objective evaluation of 140 patients, Robinson[5] concludes that ATARAX is "valuable adjunctive therapy" for patients whose dermatoses are related to emotional tension.

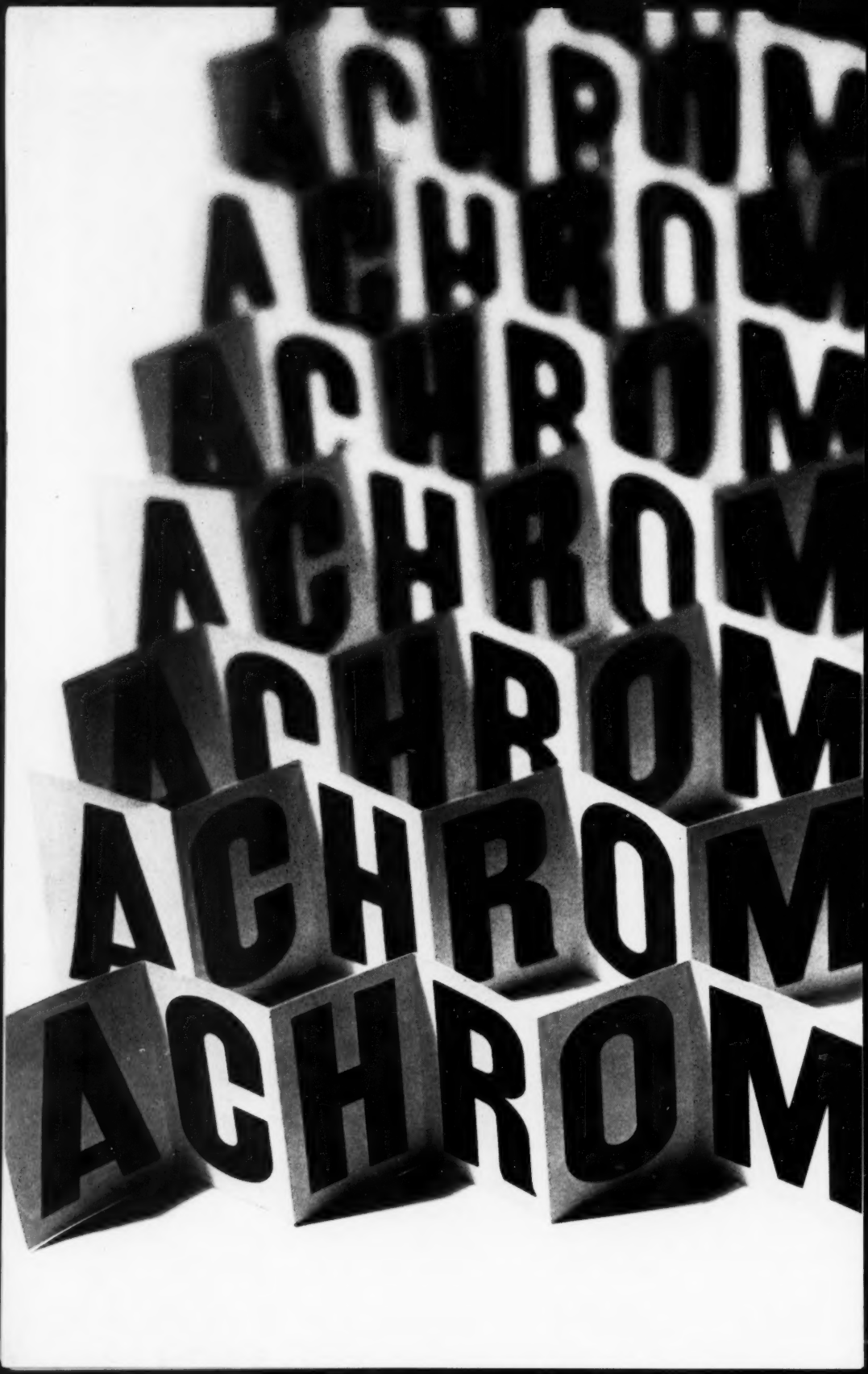
Dosage: Adults, one 25 mg. tablet, or one tbsp. Syrup q.i.d. Children, 1 or 2 tsp. Syrup t.i.d.

Supplied: Tiny 10 mg., 25 mg., and 100 mg. tablets, bottles of 100. Syrup, pint bottles. Parenteral Solution, 10 cc. multiple-dose vials.

References: 1. Feinberg, A. R., et al.: J. Allergy 29:359 (July) 1958. 2. Robinson, H. M., Jr., et al.: South. M. J. 50:1282 (Oct.) 1957. 3. Santos, I. M., and Unger, L.: Paper presented at 14th Annual Congress, American College of Allergists, Atlantic City, New Jersey, April 23-25, 1958. 4. Colrault, M., et al.: Presse méd. 64:2239 (Dec. 26) 1956. 5. Robinson, H. J., Jr., et al.: J.A.M.A. 161:604 (June 16) 1956.

Roerig Rx

New York 17, N. Y.
Division, Chas. Pfizer & Co., Inc.
Science for the World's well-being


ACHROM
ACHROM
ACHROM
ACHROM
ACHROM
ACHROM
ACHROM

Tetracycline with Citric Acid *LEDERLE*

LEDERLE LABORATORIES, a Division of AMERICAN CYANAMID COMPANY, Pearl River, New York Lederle

clinical evidence from

1,238,532

patient-days on Decadron®—

before a single prescription was written!

When you write your first prescription for DECADRON®, consider its remarkable record prior to its release.

DECADRON (dexamethasone)—on a milligram basis the most effective of all anti-inflammatory corticosteroids—is a unique product of MERCK SHARP & DOHME, pioneer and leader in corticosteroid research.

DECADRON was first synthesized in 1957. . . . In June and August, 1958, impressive clinical reports were published and presented to the medical profession[1,2,3,4,5] . . . with thousands of cases still to be published.

But only now—more than a year since the first synthesis—DECADRON is being released for general practice. During that year DECADRON was undergoing comprehensive and rigorous clinical trials by leading investigators throughout the United States. More than 1,500 patients, with every known indication for corticosteroid therapy, were treated with DECADRON and observed closely for periods up to 12 months. After the completion of a thorough objective evaluation of all the preliminary clinical trials, DECADRON is ready for your prescription.

Today you can prescribe DECADRON with confidence, because its outstanding advantages have been substantiated by extensive and prolonged clinical trials.

MERCK SHARP & DOHME

References:
1. Boland, E. W.: California Med. 88:417 (June) 1958. 2. Bunim, J. J., et al.: Arthritis & Rheumatism 1:313 (August) 1958. 3. Boland, E. W., and Headley, N. E.: Paper presented at the Annual Meeting, American Rheumatism Association, San Francisco, Cal., June 21, 1958. 4. Bunim, J. J., et al.: Paper presented at the Annual Meeting, American Rheumatism Association, San Francisco, Cal., June 21, 1958. 5. Spies, T. D., et al.: South. Med. J. 51: 1068 (August) 1958.

the crowning achievement of the first corticosteroid decade

Decadron*

DEXAMETHASONE

to treat more patients more effectively

Comprehensive and thorough clinical trials show that **DECADRON** on the milligram basis is the most effective of all oral corticosteroids ■ **DECADRON** is virtually free of sodium retention, potassium depletion, hypertension, or edema ■ **DECADRON** is virtually free of diabetogenic effect in therapeutic doses ■ **DECADRON** has not caused any new or unusual reactions ■ **DECADRON** produces neither euphoria nor depression, but restores a natural sense of well-being.

INDICATIONS: All allergic and inflammatory disorders amenable to corticosteroid therapy. CONTRAINDICATIONS: Herpes simplex of the eye is an absolute contraindication to corticosteroid therapy. DECADRON must be administered with caution in tuberculosis, other acute or chronic infections, peptic ulcer, osteoporosis, fresh intestinal anastomoses, diverticulitis, thrombophlebitis, pregnancy, and in the presence of psychotic tendencies. DOSAGE AND ADMINISTRATION: Transfer of patients from other corticosteroids to DECADRON may usually be accomplished on the basis of the following milligram equivalence:

one 0.75 mg. tablet of **Decadron*** (dexamethasone) replaces:

↓ One 4 mg. tablet of	↓ One 5 mg. tablet of	↓ One 20 mg. tablet of	↓ One 25 mg. tablet of
methylprednisolone or triamcinolone	prednisolone or prednisone	hydrocortisone	cortisone

SUPPLIED: As 0.75 mg. scored pentagon-shaped tablets. Also as 0.5 mg. tablets, to provide maximal individualized flexibility of dosage adjustment, since many patients achieve adequate control even on lower dosage.

Detailed literature is available on request.

*DECADRON is a trademark of Merck & Co., Inc.

©1958 Merck & Co., Inc.

2
TWO TYPES OF
COLLOID BATHS
FOR YOUR EVERY-DAY SKIN PROBLEMS
for standard colloid
bath therapy . . .
AVEENO*
soothing
Colloid Baths
• time-tested
• widely-accepted
*AVEENO® Colloidal Oatmeal is available in 18 oz. and 4 lb. boxes
where extra emolliency
is desired . . .
AVEENO
"Oilated"
Colloidal
Emollient Baths
for . . . the recognized soothing relief of the Aveeno Colloid Bath
PLUS . . . the emollient quality of liquid petrolatum and olive oil
AVEENO® "OILATED" (super-oiled colloidal oatmeal concentrate) is available in 10 oz. hermetically sealed cans.
AVEENO CORPORATION 250 West 57th Street New York 19, N. Y.
Distributors E. Fougera & Co., Inc.

A sense of
well being
for your
PSORIATIC
PATIENT

SOYALOID™

INDIVIDUAL DOME PACKETS

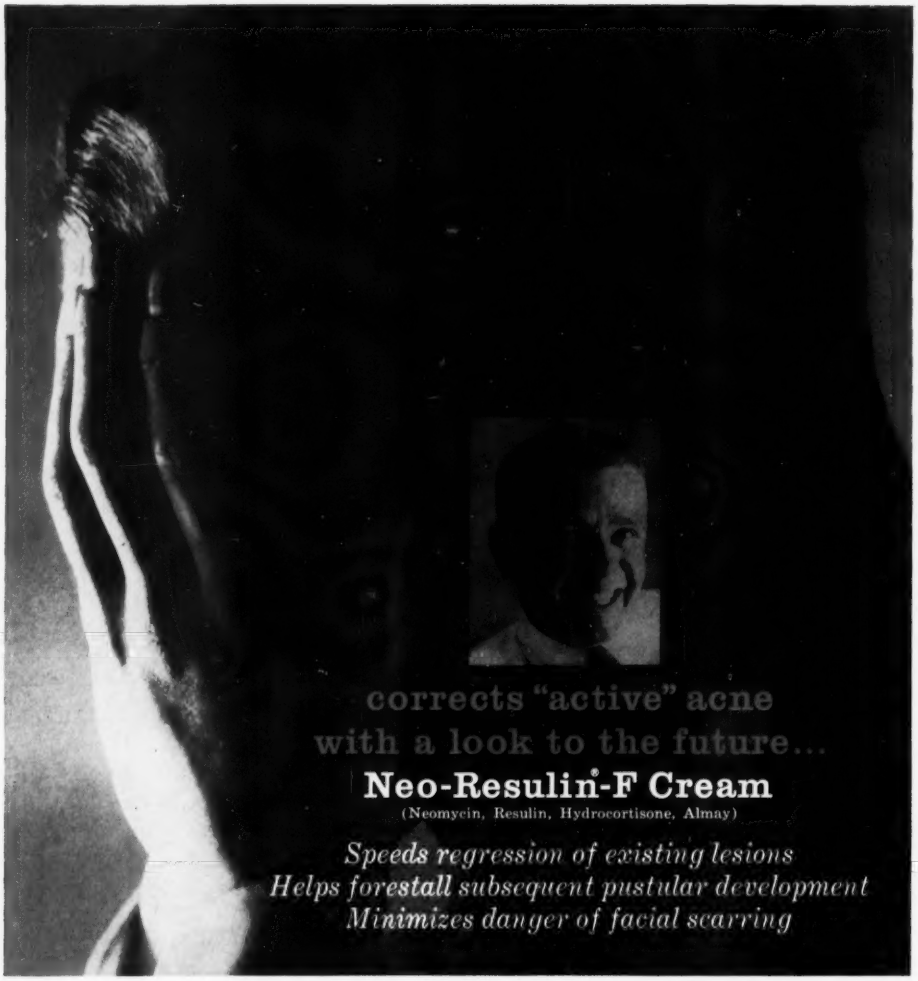
A colloid bath made with the exclusive
Soy Bean Colloid Fraction Component*
can produce a truly soothing, emollient effect—
and give the patient a feeling of well being.

A Colloid Bath with all these advantages: no stickiness—no fermentation odor—non-slippery—high in protein value (52% PROTEIN CONTENT)

Supply: Box of 5 packets, 3 oz. each

A most trusted name in Dermatologicals
DOME CHEMICALS INC.
125 WEST END AVENUE, NEW YORK 23
665 N. ROBERTSON BLVD., LOS ANGELES 46
2765 BATES ROAD, MONTREAL

*Pat. Pend'g.

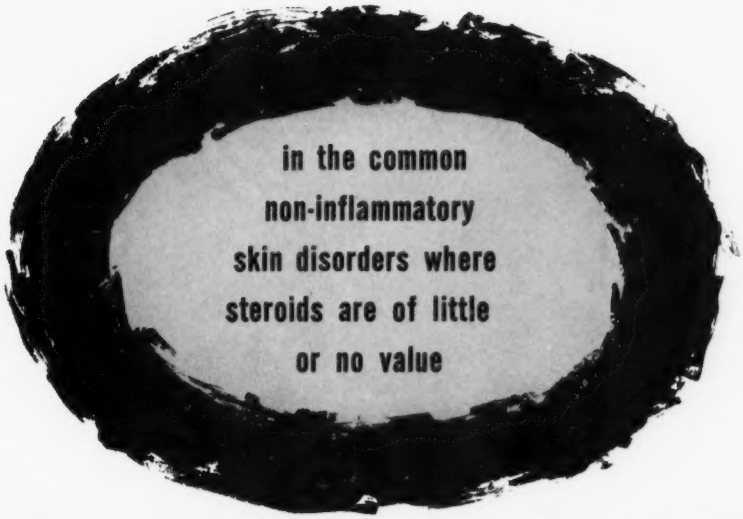

corrects "active" acne
with a look to the future...
Neo-Resulin® -F Cream
(Neomycin, Resulin, Hydrocortisone, Almay)
Speeds regression of existing lesions
Helps forestall subsequent pustular development
Minimizes danger of facial scarring

New multifaceted Neo-Resulin-F provides unusually broad corrective and prophylactic action in acne rosacea and acne vulgaris. Resorcin and sulfur supply basic keratolytic, antiseborrheic, dehydrative action. Hydrocortisone controls inflammation, hyperemia and pruritus and has been postulated to forestall hyperkeratosis at follicular openings, thus preventing subsequent occlusion. Neomycin reduces bacterial growth and clears pustular infection, thus limiting the possibility of permanent scarring.

If a topical antibiotic is not desired, Resulin-F is available without Neomycin.

Composition: Neomycin Sulfate 0.5% (equivalent to 0.35% Neomycin base); Resorcinol Monoacetate 1.5%; sulfur 2.0%; Hydrocortisone 0.5%; Alcohol by weight 8.5%. *Dosage:* Apply 3 times daily to lesions and associated skin areas. *Supplied:* 15 Gm. tubes. *Samples and Literature Available on Request*

ALMAY Division of *Schieffelin & Co.* / *Since 1794* New York 3, New York



PRAGMATAR*

an outstanding tar-sulfur-salicylic acid ointment

(including "cradle cap" and dandruff)

(including "athlete's foot," tinea capitis, etc.)

where scaling and lichenification may be a problem

following acute dermatoses of various etiologies

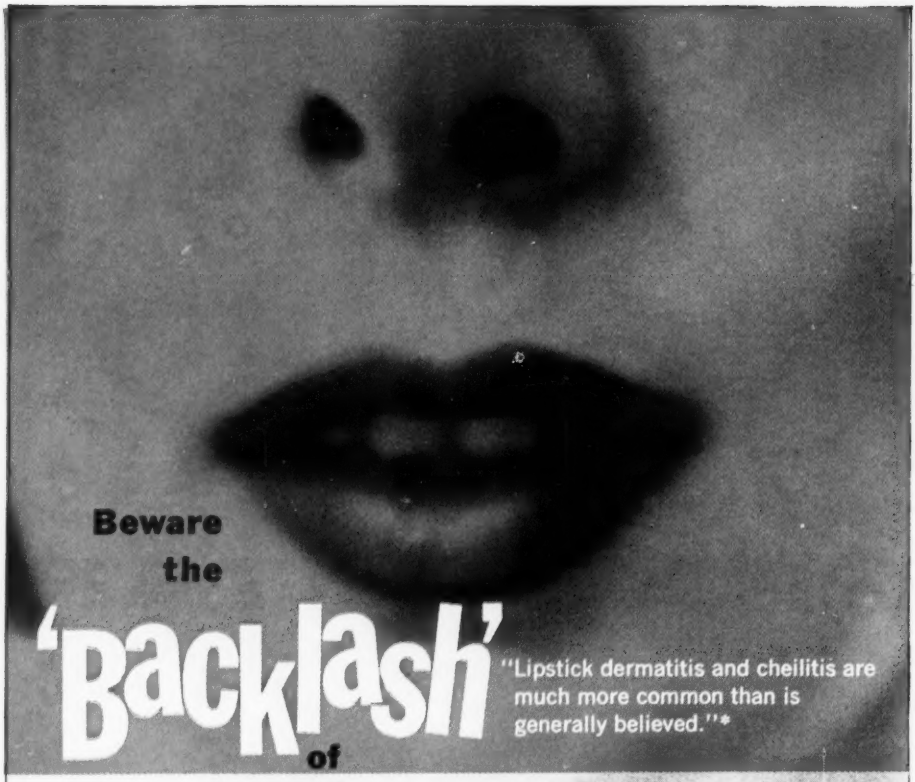
Despite the advent of topical steroids, dermatologists continually reaffirm the value of the ingredients of 'Pragmatar'. Tar, sulfur and salicylic acid remain prominent, perhaps dominant, in the management of many non-inflammatory skin disturbances.

'Pragmatar'
- exerts a prompt yet gentle keratolytic-bacteriostatic effect.
- stimulates epithelization.
- relieves itching and burning.
- holds costs down for the patient when prolonged treatment is indicated.

And 'Pragmatar', a fundamental remedy in dermatologic practice since 1943, combines its ingredients in an outstanding vehicle. 'Pragmatar' is easy to apply and remove. It does not stain. It is completely free of the "skin-preparation odor" that many patients find embarrassing. Its wide margin of safety in both adults and children is well established.

Smith Kline & French Laboratories

*T.M. Reg. U.S. Pat. Off.



Dermatoses resulting from sensitivity to a variety of lipstick ingredients can be avoided by using MARCELLE Lipsticks — another reason to remember and suggest MARCELLE® HYPOALLERGENIC COSMETICS for the patient with a cosmetic allergy or sensitivity.

MARCELLE Lipsticks — available in a full range of colors — are offered in different formulas to eliminate common sensitizers, and to avoid perfumes and the bromofluoresceins. The MARCELLE Lipstick Testing Kit, providing 14 different formulations, enables you to help your patient select a lipstick best suited to her case.

Marcelle COSMETICS

Borden's PHARMACEUTICAL DIVISION
350 Madison Avenue, New York 17

Available in Canada through Prof. Sales Corp., Montreal

*Zakon, S. J., et al.: Arch. Dermat. & Syph. 56:499, 1947; abstracted in Birmingham, D. J., and Campbell, P. C., Jr.: Occupational and Related Dermatoses, U. S. Public Health Service Publication No. 364, 1954.

YOUR PATIENT?

ALLERGIC EMERGENCY—INJECTION HYDELTRASOL dramatically relieves pain, inflammation, discomfort, itching, and distress . . . permits the patient to rest and sleep.

ACUTE ASTHMATIC—INJECTION HYDELTRASOL promptly suppresses the bronchospasm—reduces the number of asthmatic attacks, dyspnea and wheezing—restores functional capacity.

In your bag . . .
ready for use . . .
IMMEDIATELY!

THE FIRST READY-TO-USE,
SOLUBLE,
ALL-PURPOSE
PARENTERAL STEROID

INJECTION HYDELTRASOL®

(Prednisolone 21-Phosphate)

ADVANTAGES:

1. Immediately effective—dramatic response in minutes
2. Ready for use—needs no reconstitution or refrigeration
3. In solution—flows readily through a small-bore needle

SUPPLIED: In 2-cc. and 5-cc. vials, each cc. containing 20 mg. of prednisolone 21-phosphate as the di-sodium salt.

Hydeltrasol is a trademark of Merck & Co., Inc.

MERCK SHARP & DOHME DIVISION OF MERCK & CO., INC., Philadelphia 1, Pa. MSD

DISPERSE!

A military tactic is added to the dermatologist's armamentarium

American rebels taught British Redcoats the value of dispersing during the Revolutionary War. This deployment increased the area one man could cover effectively—while decreasing the risk. By dispersing their troops, the shrewd Yankees successfully harried the rigidly maintained columns of King's Regulars at every turn.

Medical science has borrowed this tactic of dispersion to make safer the use of one of dermatology's most effective weapons—crude coal tar. Crude coal tar's usefulness is undisputed, but the high incidence of irritation resulting from its use has caused many doctors to prescribe it only sparingly, if at all.

Postulating that the large tar particle size (up to 100 microns) in crude coal tar could be partially responsible for the irritation, Pflag and Zopf (1) discovered the means to reduce the tar particles to about 3 microns. Further reasoning led Carney and Zopf (2) to believe that a lower concentration of this minutely dispersed coal tar would be as effective as the commonly prescribed 2% to 5% preparations of ordinary tar. Clinical studies upheld their theory. Thus, the dispersion of the smaller tar particle size in a lower concentration resulted in a greatly lowered incidence of irritation without diminution of its therapeutic effectiveness —indeed an important addition to the dermatologist's armamentarium.

Dispertar Ointment, made according to the Carney and Zopf method, provides 1% coal tar and 0.5% polyoxyethylene sorbitan monolaurate (solutar) in an oleaginous base which adheres well to the skin, protects against chemical and mechanical trauma, is occlusive and gives some lubrication. Tests prove Dispertar Ointment may be prescribed freely and the trend is to its use on active, acute dermatitis.

For more detailed information and sample of

DISPERTAR OINTMENT

write to:

TEXAS PHARMACAL COMPANY

San Antonio, Texas

1. Pflag, S.C. and Zopf, L.C.; Hydrophilic Forms of Tars; *U. S. Armed Forces M. J.* 2:1177-1181 (Aug.) 1951.

2. Carney, R.G. and Zopf, L.C.; An Improved Coal Tar Ointment Using a Surfactant, *Arch. of Dermat.* 72:266-271 (Sept.) 1955.

now, for the first time, **liquid** meprobamate

Equanil® Suspension

Meprobamate, Wyeth

Wyeth

Philadelphia 1, Pa.

acceptably flavored . . .

your answer to tablet problems in anxiety and tension states

- in children
- in the aged
- in all patients who reject tablet medication

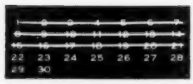
Conforms to Code for Advertising

SUPPLIED: Suspension, 200 mg. per 5-cc. teaspoonful, bottles of 4 fluidounces. Also available: Tablets, 400 mg., scored, bottles of 50; 200 mg., scored, vials of 50. WYSEALS® EQUANIL, tablets, 400 mg., vials of 50.

RELIEVES TENSION—MENTAL AND MUSCULAR

QUICK RELIEF...3 DAYS

RAPID HEALING...3 WEEKS



for PRURITUS ANI

orally treated with . . . . Borcherdt

MALT SOUP EXTRACT

More and more physicians are telling us of the successful results from treating Pruritus Ani orally with Borcherdt's Malt Soup Extract. The intractable itching disappears in three or four days and the perianal skin becomes normal in three or four weeks. Even stubborn cases of many years standing usually yield or show marked improvement.

Malt Soup Extract is a non-diastatic barley malt extract neutralized with potassium carbonate. Most importantly, it promotes aciduric bacteria in the lower intestine, creates easily passed stools and overcomes, in a natural way, the alkaline condition so prevalent in cases of Pruritus Ani.

There are no side effects; no drug fastness, no gas pain. Malt Soup Extract is a food not a drug. Results are secured naturally and once attained medication can be discontinued or greatly reduced.

Malt Soup Extract is available in 8 and 16 ounce jars at most pharmacies coast to coast.

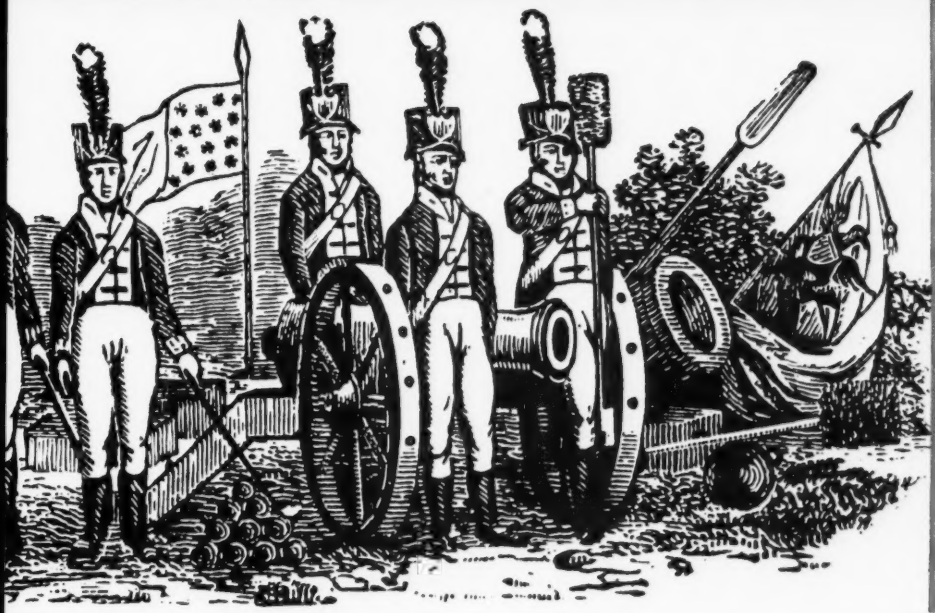
We will gladly send you samples and descriptive literature

BORCHERDT COMPANY

217 North Wolcott Avenue, Chicago 12, Illinois

In Canada, Chemo Drug Co. Ltd., Toronto, Canada

SERVING THE MEDICAL PROFESSION SINCE 1868



N THE WAR *on inflammatory and allergic dermatoses*

METI-DERM Aerosol
METI-DERM Cream 0.5%

THE DERMATOLOGIST'S WEAPONS

launching an all-out attack on the itching, burning, swelling, oozing of pathologic skin conditions with the antiallergic, anti-inflammatory, antipruritic action of prednisolone—approximately twice as effective, milligram for milligram, as topical hydrocortisone.

offering an arsenal of "Meti" steroid benefits in the form preferred by many dermatologists

nonsensitizing — nonstaining
nonocclusive — water washable
cosmetically acceptable

METI-DERM Aerosol—"hands-off" therapy sprayed directly on offending lesions for instant, cooling itch-relief...enables dermatologist to treat hard-to-reach areas before patient leaves office.

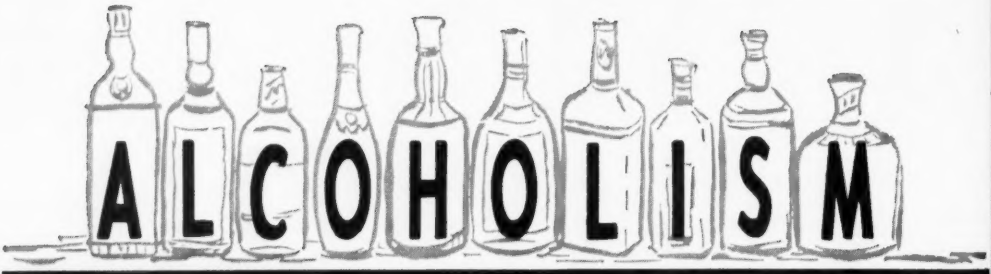
METI-DERM Cream 0.5%—for those who prefer a cream base.

METI-DERM,® brand of prednisolone topical.
Meti,® brand of corticosteroids.

Schering

SCHERING CORPORATION • BLOOMFIELD, NEW JERSEY

MD-J-429



an important problem in today's living...

The following articles from TODAY'S HEALTH are now available in pamphlet form.

ALCOHOLISM IS A DISEASE. A discussion by the Chairman of the A.M.A. Committee on Alcoholism. by Marvin A. Block, M.D., 8 pages, 15 cents.

I AM THE WIDOW OF AN ALCOHOLIC. Three articles combined. by Virginia Conroy, 16 pages, 20 cents.

HOW EXPERTS MEASURE DRUNKENNESS. A partial transcript of an actual courtroom case. by H. A. Heise, 8 pages, 15 cents.

BARBITURATES, BOOZE AND OBITUARIES. A discussion of the dangers of mixing alcohol and barbiturates. by Donald A. Dukelow, 4 pages, 10 cents.

TWELVE STEPS FOR ALCOHOLICS. A frank discussion of the meaning of an alcoholic behavior. by Richard Lake, 6 pages, 10 cents.

These articles are available in one pamphlet for 50c

ALCOHOLICS ANONYMOUS. Written from the standpoint of a member, the basic treatment procedures are described and the psychological problems confronting the alcoholic are discussed.

ALCOHOL AND CIRRHOSIS OF THE LIVER. Relationship between alcohol, diet and cirrhosis. Increasing stress on nutritional differences. by Russell S. Boles.

HOW TO HELP A PROBLEM DRINKER. Understanding the alcoholic's capabilities, the necessity of help, causes of his condition. by Edward A. Strecker and Francis T. Chambers, Jr.

THE TREATMENT OF ALCOHOLISM. Tracing the steps from convincing the alcoholic that he is sick through treatment and cure. by Lewis Inman Sharp.

CONDITIONED REFLEX TREATMENT OF CHRONIC ALCOHOLISM. Its place among methods of treatment today, its development and correlation with personality factors. by Walter L. Voegtlin.

INSTITUTIONAL FACILITIES FOR THE TREATMENT OF ALCOHOLISM. Comparative differences, in drinking, with the last century, new establishments and methods of treatment, lack of trained personnel. by E. H. L. Corwin.

ADDRESS REQUESTS TO

ORDER DEPARTMENT

AMERICAN MEDICAL ASSOCIATION

535 N. DEARBORN ST., CHICAGO 10, ILLINOIS

Specific Antihistaminic Effect
reduces—erythema, excoriation and extent of lesions[1-4]

Recommended Oral Dosage:
50 mg. q.i.d. initially; adjust according to individual response.

References: 1. Feinberg, A. R., et al.: J. Allergy *29*:358 (July) 1958. 2. Eisenberg, B. C., Clinical Medicine *5*:897-904 (July) 1958. 3. Robinson, H. M., et al.: J.A.M.A. *161*:604-606 (June 16) 1958. 4. Robinson, H. H., et al.: So. Med. J. *50*:1282 (Oct.) 1957.

*Trademark

Psychotherapeutic Potency
relieves—tension, anxiety and itching.[1-4]

Supplied as:
Vistaril Capsules—25 mg., 50 mg., 100 mg.
Vistaril Parenteral Solution—10 cc. vials and 2 cc. Steraject® Cartridges, each cc. containing 25 mg. hydroxyzine (as the HCl)

Pfizer *Science for the world's well-being*

PFIZER LABORATORIES Division, Chas. Pfizer & Co. Inc., Brooklyn 6, N. Y.

No one asked me to play... before COVERMARK®

Covermark conceals dermatological blemishes.

Children are cruel to each other. Any child who is different is often ridiculed, rejected . . . and may not be asked to play. This is particularly true of the youngster with an unsightly birthmark. Because such children are sensitive, they often become sullen, unhappy, and difficult to manage. They may develop problem personalities. When parents seek medical aid, and the condition cannot be resolved by plastic surgery or other measures, it is then suggested that you recommend **Waterproof Covermark.**

Waterproof Covermark effectively conceals various types of skin discolorations, whether permanent or temporary. It is a neutral cream, opaque, waterproof and will not crack or flake.

Covermark can be used to conceal nevi of various types, as in vitiligo, post-operative scars, papules or pustules, varicose veins and various types of skin blemishes.

Easy to apply: **Covermark** supplied in eight shades – to match all normal skin tones.

Case History

Female patient, age 7, with extensive facial discoloration. Upon examination surgery was contraindicated. Parent was instructed to apply Waterproof Covermark. Extreme improvement in appearance was noted.

How Supplied: **Waterproof Covermark** is supplied in 1 oz.-3¼ oz. jars. **Covermark,** in waterproof form may be used when the patient goes swimming, or is subject to much perspiration.

NOTE: Minor skin blemishes are easily concealed with Spotstick – which is **Waterproof Covermark** in stick form.

PROFESSIONAL DATA supplied to physicians upon request. Available on your recommendation, through your pharmacist, and at leading department stores.

(After) Photograph of child, L.R., Covermark applied.

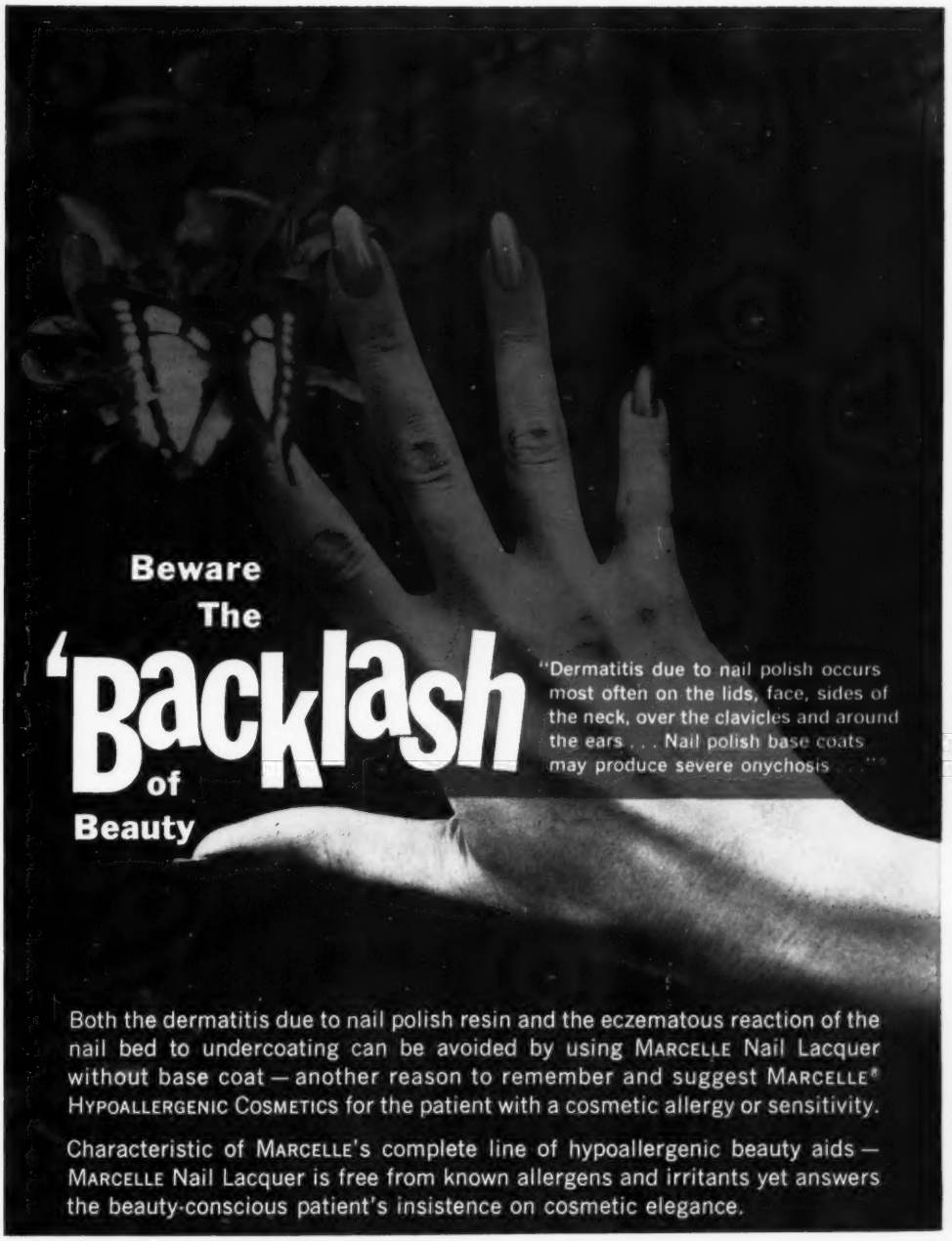
These are unretouched photographs of an actual case.

Lydia O'Leary

For more detailed information write direct to:

Department A

INC. 41 East 57th Street, New York 22, New York


Beware
The
'Backlash
of
Beauty
"Dermatitis due to nail polish occurs most often on the lids, face, sides of the neck, over the clavicles and around the ears . . . Nail polish base coats may produce severe onychosis"*

Both the dermatitis due to nail polish resin and the eczematous reaction of the nail bed to undercoating can be avoided by using MARCELLE Nail Lacquer without base coat — another reason to remember and suggest MARCELLE® HYPOALLERGENIC COSMETICS for the patient with a cosmetic allergy or sensitivity.

Characteristic of MARCELLE's complete line of hypoallergenic beauty aids — MARCELLE Nail Lacquer is free from known allergens and irritants yet answers the beauty-conscious patient's insistence on cosmetic elegance.

Marcelle COSMETICS

Borden's PHARMACEUTICAL DIVISION
350 Madison Avenue, New York 17

Available in Canada through Prof. Sales Corp., Montreal

*Andrews, G. C.: Diseases of the Skin, ed. 4, Philadelphia, Saunders, 1954, pp. 117, 118

Never before in ACNE!

Graded long-term abrasion

The 3 grades of BRĀSIVOL permit a logical 3-step course of therapy:

1

Mild abrasion for 2-4 weeks with BRĀSIVOL FINE

2

More vigorous abrasion for 2-4 weeks with BRĀSIVOL MEDIUM

3

Maintenance treatment for as long as needed with BRĀSIVOL ROUGH

BRASIVOL introduces a new concept in the treatment of acne: prolonged superficial abrasion precisely adjustable to the patient's progress. Ten years of clinical studies in over a thousand acne patients have demonstrated the success of continuous abrasion in maintaining patency of the sebaceous ducts by gentle desquamation, thereby reducing comedones, papules, pustules and cysts, and minimizing post-acne scarring.

BRASIVOL contains non-silicon abrasives (fused synthetic aluminum oxide) of carefully selected particle sizes and in appropriate ratios, with hexachlorophene 1.0%, in a specially formulated base of soap and synthetic detergent.

1. Saperstein, R. B.: Presented at 107th annual meeting of American Medical Assn., San Francisco, Calif., June 23-27, 1958.

SUPPLIED:
Jars of Brāsivol Fine 6 oz.; Brāsivol Medium 6½ oz.; Brāsivol Rough 7 oz.

Brāsivol™

GRADED ABRASIVE CLEANSER FOR ACNE

Write for samples and informational literature

STIEFEL LABORATORIES, INC.
Oak Hill, New York

Canadian representatives:
WINLEY-MORRIS CO., LTD., Montreal 29, Quebec

FOUNDED 1847 **STIEFEL®**

FRIGIDERM®

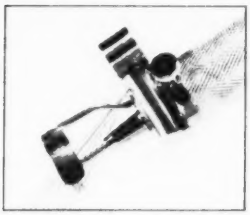
(100% dichloro-tetrafluoro-ethane...contains no ethyl-chloride)

SKIN REFRIGERANT—ANESTHETIC

*Widely Accepted for Local Anesthesia in Surgical Planing of the Skin**

JET-SPRAY PLANER

This hand-tooled, precision-built instrument with diamond fraises is available for most standard planing units. In ordering, please specify make of planing unit. Full information on request.



FRIGIDERM has been researched and developed to meet the expressed need of physicians for a well tolerated skin refrigerant-anesthetic...non-explosive, non-inflammable...having no general anesthetic properties.

Today, **FRIGIDERM** is one of the preferred products of its kind among Dermatologists everywhere.

FRIGIDERM quickly produces local anesthesia for surgical planing in the treatment of scarring due to acne, chickenpox, smallpox and trauma...multiple senile keratoses...fine wrinkling...traumatic tattoos.

Also for incision of furuncles, electrocautery to small cutaneous tags, flat warts, or for alleviation of needle pain during hypodermic injection.

This freezing agent can be delivered from the spray-top container shown above by easy finger pressure.

Now in the improved 8 oz. container — $2.00

Fully guaranteed for satisfactory performance
Available at your surgical supply dealer

*A.M.A. Archives of Dermatology, April 1955
Ref.: Wilson, J. W.; Laikari H, R.; Ayres III, S., Reprints available*

® REGISTERED TRADE MARK

W. T. BRACHVOGEL

1723 WEST SEVENTH STREET • DUNKIRK 4-9273 • LOS ANGELES 17, CALIFORNIA

DROUGHT RELIEF

for dry skin

LUBRIDERM*

topical application

Individuals suffering from parched, dry skin find immediate relief with soothing Lubriderm, a carefully balanced oil-in-water emulsion. As Lubriderm's aqueous outer-phase helps restore suppleness to drawn, taut skin, the oily inner-phase softens roughened, chapped areas and acts as a protective barrier to the further loss of moisture. When used persistently, Lubriderm insures a soft, smooth, comfortable skin condition.

*Contains cholesterol derivative of lanolin.

Lubath

bath additive

Many persons with dry skin experience bothersome itching and burning of the skin after bathing, a discomfort which generally worsens whenever the humidity of the air is low. Such after-bath pruritus is often controlled with the use of Lubath in the bath water. Lubath, a highly refined cottonseed oil made dispersible in hard or soft water by a non-irritating, non-ionic surfactant, deposits a thin film of oil over the entire body while bathing, usually bringing prompt relief.

For detailed information and samples, write . . .

TEXAS PHARMACAL COMPANY

San Antonio, Texas

For acne and pimples with extensive flush areas

Acne Cort-Dome™

Hydrocortisone with sulfur, bithionol, resorcinol monacetate, in aluminum acetate vehicle pH 5.0

CREME or LOTION

DOME

antiinflammatory/keratolytic

INCORPORATED IN EXCLUSIVE ACID MANTLE VEHICLE ®

Within a short period of time suppresses the epidermatitis of acne, reduces erythema, allays inflammation, soothes acute exacerbations and produces enough peeling action to gently open the papules and pustules. Restores and maintains normal acidity of the skin.

SIG: Apply morning and night to skin after washing and at night to scalp.

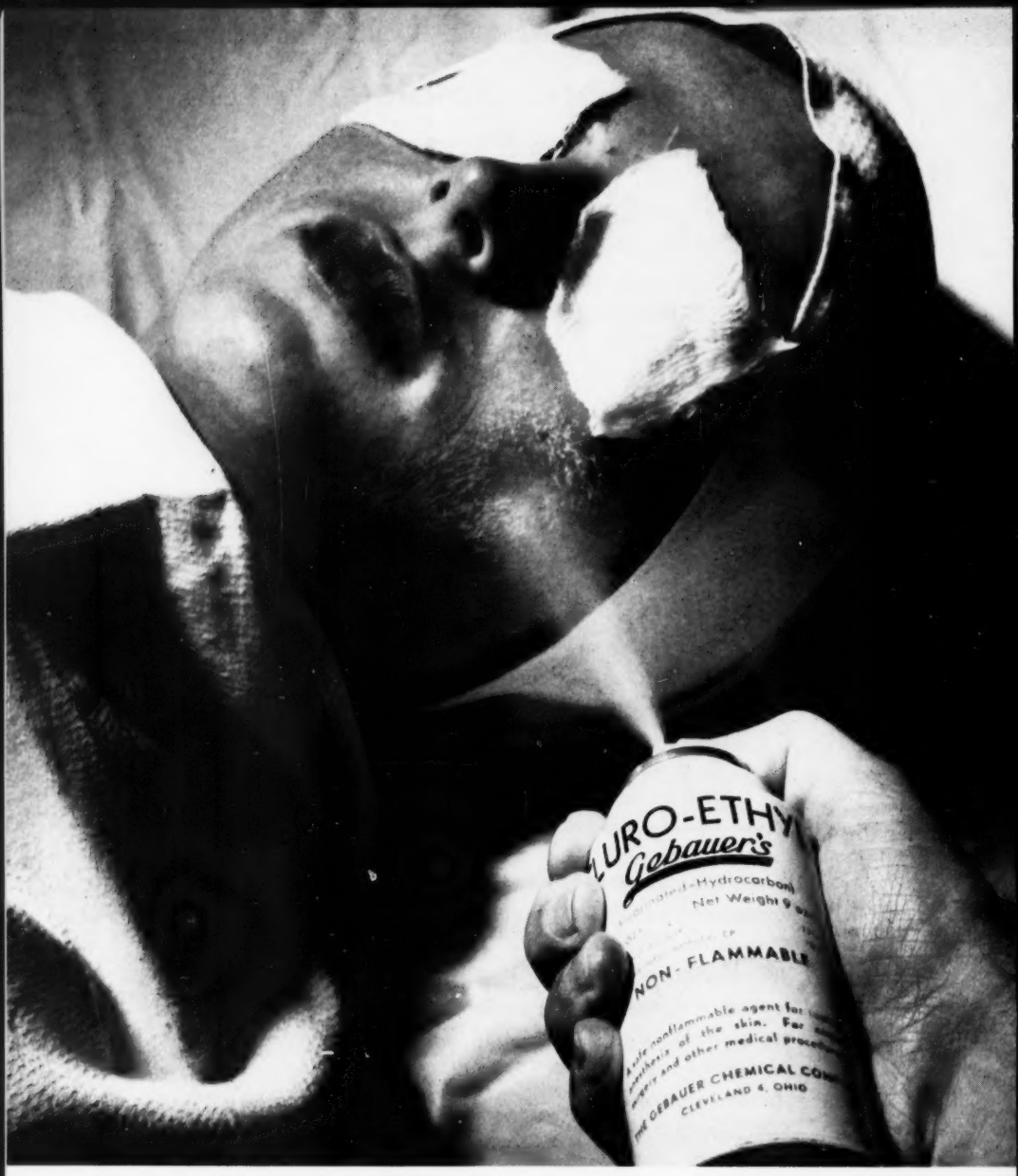
SUPPLY: Creme in 1 oz. tubes. Lotion in 1 oz. squeeze bottles. Samples and literature on request.

DOME CHEMICALS INC.

NEW YORK 23 LOS ANGELES 46

IN CANADA: 2765 BATES RD., MONTREAL, P. Q.

A TRUSTED NAME IN DERMATOLOGICALS



The improved, new local anesthetic The evidence is mounting: many able dermatologists are now convinced th new Fluro-Ethyl is a preferred most efficient refrigerant for skin planing. An actual report: "I have used your mixture of 25 Ethyl Chloride and 75% Freon for skin planing, and I find it most satisfactory; freezing is fast, each container lasts a long tim results of the planing are completely satisfactory to me." Why is Fluro-Ethyl so efficient? Because this non-flammable, azeotrop mixture combines high pressure with low boiling point, and negligible irritation to the skin. May we suggest that you compare with any other product? Gebauer Chemical Company, 9410 St. Catherine Avenue, Cleveland 4, Ohio.

FLURO-ETHYL

GEBAUER

CHEMICAL COMPANY

THE THOUSAND WAYS... AND WHYS... OF TARBONIS®

for unexcelled COAL TAR Therapy

Few medications are more firmly entrenched in dermatologic therapeutics than coal tar. And few indeed have more diverse demands made upon them. TARBONIS, as the sole active agent or as a component of dermatologic prescription formulations, helps to achieve prompt remissions in a wide range of common dermatoses.

TARBONIS, tar therapy unexcelled in performance and acceptability, is a special, refined extract of coal tar in an exclusive vanishing cream base.

UNSURPASSED IN EFFECTIVENESS—promptly relieves itching and promotes healing.

VERSATILE—An excellent vehicle for individualized prescription formulas.

COSMETICALLY ELEGANT—No tarry color, no mess, no stain.

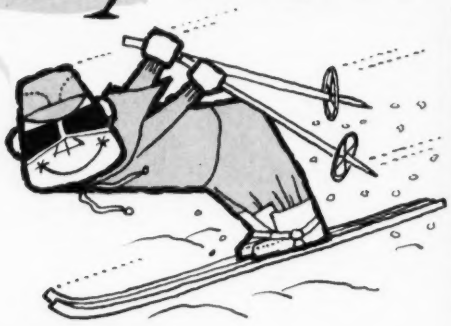
TARBONIS CREAM: 5% Special Coal Tar Extract in an Exclusive Vanishing Cream Base.

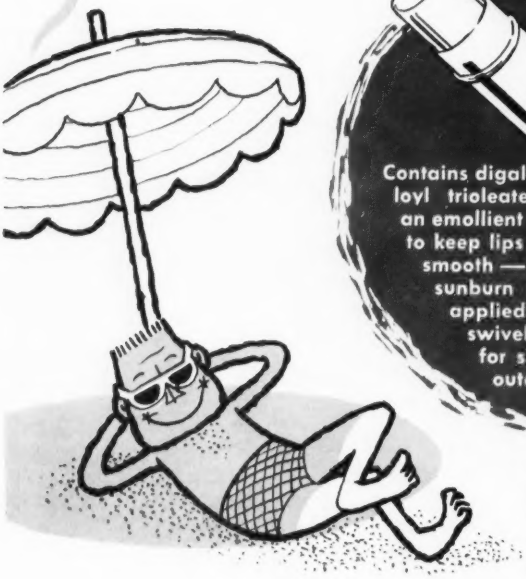
Available at all pharmacies on prescription in jars of 2¼ oz. and 1 lb.

REED & CARNRICK · *Jersey City 6, New Jersey*

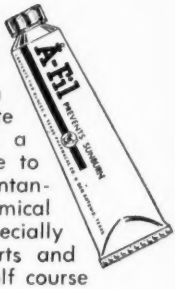
under any sun!

A-Fil® sun products help your patients enjoy their time in the winter sun — whether it's spent on the mountain slopes where the ultraviolet rays are the most harmful — or on the sunny beaches of the warmer climes.





A-Fil®
SUN STICK
A-Fil
SUN STICK
Contains digalloyl trioleate in an emollient base— to keep lips soft and smooth — and free from painful sunburn and windburn. Easily applied with the handy new swivel type case. Ideal for skiing, fishing, any outdoor activity.



A-Fil® Sun Protective Cream contains menthyl anthranilate and titanium dioxide in a vanishing cream type base to prevent sunburning and suntanning through complete chemical and physical protection. Especially suitable for mountain sports and extra long hours on the golf course or at the beach.

Neo A-Fil®
contains digalloyl trioleate in a non-tinted, emollient, vanishing cream type base. Prevents sunburning, but promotes suntanning. For individuals wanting something to show for the hours spent in the sun.

Allercreme®

Saf-Tan® Cream
a special "cosmetic" package of Neo A-Fil®, slightly more perfumed, particularly appealing to women.

For further details or a complimentary stock size package of any A-Fil® sun product for your personal winter sun protection, write . . .

Texas Pharmacal Company
San Antonio, Texas

Fostex®
treats their acne while they wash

degreases the skin helps remove blackheads dries and peels the skin

...and this is how it works

Fostex provides essential actions necessary in treating acne. It washes off excess oil. It unblocks pores by penetrating and softening blackheads. It dries and peels the skin, removing papule coverings, thus permitting drainage of sebaceous glands.

Fostex contains Sebulytic®,* a combination of surface-active wetting agents with remarkable antiseborrheic, keratolytic and antibacterial actions . . . enhanced by sulfur 2%, salicylic acid 2%, hexachlorophene 1%.

*sodium lauryl sulfoacetate, sodium alkyl aryl polyether sulfonate and sodium dioctyl sulfosuccinate.

Your patients will like Fostex because it is so simple to use. They simply wash acne skin 2 to 4 times a day with Fostex, instead of using soap.

FOSTEX CREAM

. . . in 4.5 oz. jars. For therapeutic washing in the initial phase of oily acne treatment.

Write for samples.

FOSTEX CAKE

. . . in bar form. For therapeutic washing to keep the skin dry and free of blackheads during maintenance therapy. Also used in relatively less oily acne.

WESTWOOD PHARMACEUTICALS • **Buffalo 13, New York**

"...soothing and nonirritating and especially helpful in allaying the itching."*

Prophyllin® wet dressings

PROPHYLLIN combines sodium propionate and water-soluble chlorophyll derivatives in a wet dressing of unusual effectiveness. Complete healing or significant improvement in over 100 patients with various dermatologic lesions led the reporting physicians* to state: "It (PROPHYLLIN) seems to be particularly useful because of its (a)...physiologic action; (b) lack of toxicity; (c) bacteriostatic and fungistatic properties, and (e) soothing, healing, and especially antipruritic effects."

particularly useful in acute contact dermatitis

In 40 cases, PROPHYLLIN was considered "...a wet dressing of choice, even where there was some secondary infection."*

PROPHYLLIN Powder, for preparation of wet dressings, in cartons of 12 packets. (Each packet contains 2.3 Gm. of powder, sufficient to prepare 8 ounces of solution containing 1 per cent sodium propionate and 0.0025 per cent water-soluble chlorophyll.) Also in 4-ounce and 16-ounce jars.

PROPHYLLIN Ointment, in 1½-ounce and 4-ounce tubes. (PROPHYLLIN Ointment contains 5 per cent sodium propionate and 0.0125 per cent water-soluble chlorophyll.) Provides the benefits of PROPHYLLIN for ambulatory patients and where a wet dressing is contraindicated or impracticable.

*Peck, S. M.; Traub, E. F., and Spoor, H. J.: A.M.A. Arch. Dermat. & Syph. 67:263, 1953.

Rystan company Mount Vernon, N. Y.

27857

A.M.A. ARCHIVES OF
DERMATOLOGY

Keratoacanthoma

Experimentally Induced with Methylcholanthrene in the Chicken

R. H. RIGDON, M.D., Galveston, Texas

In 1934, Ferguson Smith [1] described a self-healing squamous-cell epithelioma in the skin of a man 23 years of age. In 1955, Ereaux and associates [2] reported a case in which there were widespread self-healing epithelial tumors in the skin of a white man 41 years of age that were considered keratoacanthomas. The clinical and histologic characteristics of this lesion have been described.[2-18] A new classification of keratoacanthomas in three histological types, Types 1, 2, and 3, has been suggested recently by Ghadially.[19]

In considering the etiology of the localized type of keratoacanthoma, Anderson,[2] in the discussion of Ereaux's paper, says, "One is impressed . . . as to the frequent history of preceding trauma, such as a cut, scratch, or the squeezing of a blackhead. There is no doubt that very similar, if not identical, lesions occur in those exposed to tar." Actinic or oil sensitization has been implicated,[16] also sunlight [18] and oil and tar.[4] There are observations that would suggest a viral origin.[2] Since some of the cases have been observed in members of a family, there may be a genetic factor.[3,17]

Submitted for publication July 29, 1958.

Professor of Pathology, The University of Texas—Medical Branch.

This study was aided by research Grants C-1469 (C-5) from the National Cancer Institute of the National Institutes of Health, Public Health Service, and from the Tobacco Industry Research Committee.

In the study of carcinogenesis in the chicken,[20-22] we have observed lesions in the skin following local applications of methylcholanthrene characterized by a macule that subsequently progressed in size and ulcerated. Histologically, the lesion has all the characteristics of a squamous-cell carcinoma, but it spontaneously regresses. This lesion in the chicken is described at this time because of its similarity to keratoacanthoma.

Methods and Material

The technique used to produce these tumors has been reported.[20] A 0.25% solution of methylocholanthrene in acetone was applied to the skin of the body beneath the wing and to the undersurface of the wing. The acetone solution of methylcholanthrene, 0.2 ml., was used on the day-old chicks, and 1 ml. was used on the older birds. The applications of the carcinogen were made daily, except for Saturdays and Sundays. The total number of applications for any one bird varied from 1 to 30. In some experiments the feathers were plucked, either before, during, or after the methylcholanthrene was applied. The lesions sometimes were either biopsied or completely excised for histologic study.

Results

The details of the experimental observations made in this study have been reported.[20,21] The earliest tumor occurred 23 days after the first application of methylcholanthrene. The longest interval between the first application of methylcholanthrene and the development of a tumor was 128 days. Eight was the largest number of

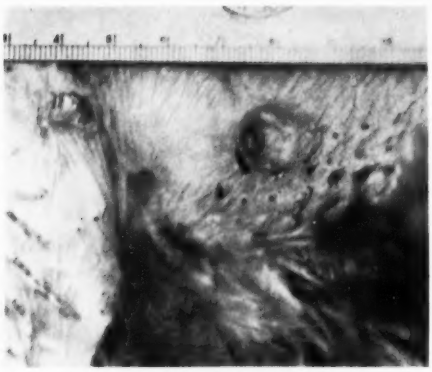


Fig. 1.—The center of these squamous-cell tumors is filled with keratin. Hematoxylin and eosin; reduced 20% from mag. × 19.

tumors observed at one time in any one chicken. The lesions, when first observed, were nodules about 2 mm. in diameter. They progressively grew, and their centers were filled with keratin (Fig. 1). They subsequently ulcerated (Figs. 2, 3, and 4). The size of the ulcers varied from 3 to 12 mm. The base was granular; the periphery was hyperplastic, and the edges were undetermined. Healing seemed to progress rapidly from both the base and the periphery; a typical scar resulted.

Histologically, the lesion always was characterized by squamous cells (Fig. 5). Intercellular bridges (Fig. 6) were conspicuous in some, while in others typical epithelial pearls were present. Keratin and mitotic cells were numerous in some of the lesions (Figs. 7 and 8). Polymorphonuclear leukocytes were present in the crater of the tumors. Leukocytes, mononuclear cells, and groups of lymphocytes were present in the surrounding dermis (Figs. 9 and 10). Polymorphonuclear leukocytes frequently were prominent about the periphery of the tumor. Extensive degeneration occurred in the squamous cells at the periphery of the growth (Fig. 11). The degree of degeneration varied in the different lesions, both within the same chickens and in different birds. Ultimately, the squamous cells in the tumor completely degenerated; the leukocytes phagocytized the debris, and collagen fibers filled the area.

This degenerative change in the tumor is most pronounced and seems to begin at the periphery of the growth. It proceeds inward until all the epithelial cells are destroyed. The time for regression varied from two weeks to two months.

Comment

The tumors that develop in the skin of chickens following the local application of methylcholanthrene resemble in many ways the keratoacanthoma described in man by McNulty and Sommers.[16] They have described this lesion as follows:

Fig. 2.—This chicken was 77 days of age when 1.0 ml. of the solution of methylcholanthrene was applied daily for 30 days except for Saturdays and Sundays. The lesion was first observed on the 75th day after the first application of methylcholanthrene. Photographed on the 99th day.

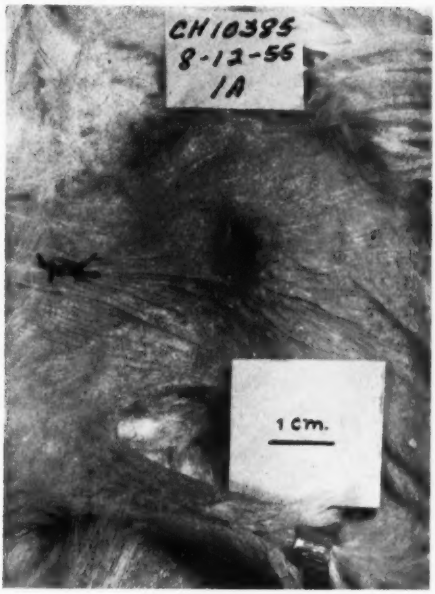


Fig. 3.—Treated same as chicken shown in Figure 1. Photographed on the 105th day after the first application of methylcholanthrene.

Fig. 4.—Treated same as chicken shown in Figure 1. Photographed on the 47th day after the first application of methylcholanthrene. The tumor was 1.0 cm. at this time.

. . . crateriform, with masses of keratin packed in centrally and superficially . . . On section the mass is pulpy, moist, keratinaceous, exudes a cloudy fluid, and has a crumbling yellow-brown appearance . . . rounded masses of partly keratinized cells with abundant ground-glass-like eosinophilic cytoplasm and prominent intercellular bridges are bulging downward into the dermis and everting the marginal unaffected epithelium . . . . The basement membrane boundary zones are obscured or lost, and a heavy infiltrate of leucocytes surrounds and overflows into the epithelial downgrowths . . . . Under higher magnification the diffuse mingling of leucocytes, particularly neutrophils, eosinophils, and lymphocytes, with sheets of epithelium is further emphasized . . . . Plasma cells, lymphocytes

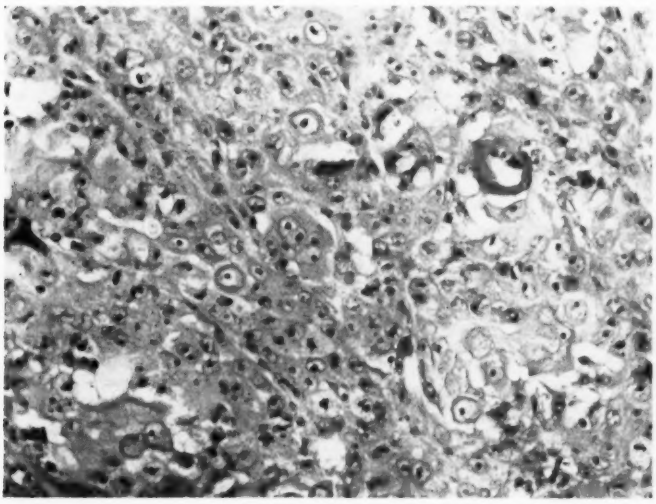


Fig. 5.—The squamous epithelial cells vary in size and shape. Epithelial pearls do occur. Mitotic figures are present. Hematoxylin and eosin; reduced 10% from mag. ×340.

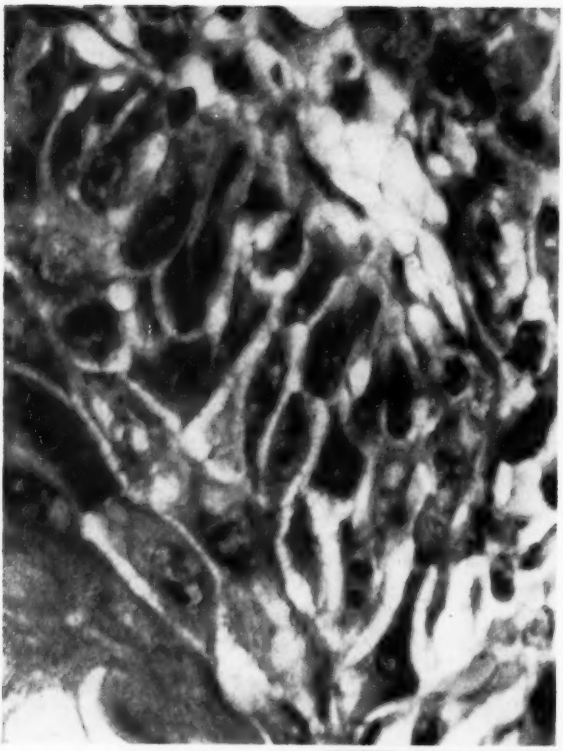


Fig. 6.—Intercellular bridges are present in some of these squamous-cell tumors in the chicken. Hematoxylin and eosin; ×800.

Fig. 7.—These are groups of squamous cells with ground-glass-like eosinophilic cytoplasm in focal areas of these tumors. Observe the large number of polymorphonuclear leukocytes. Hematoxylin and eosin; ×340.

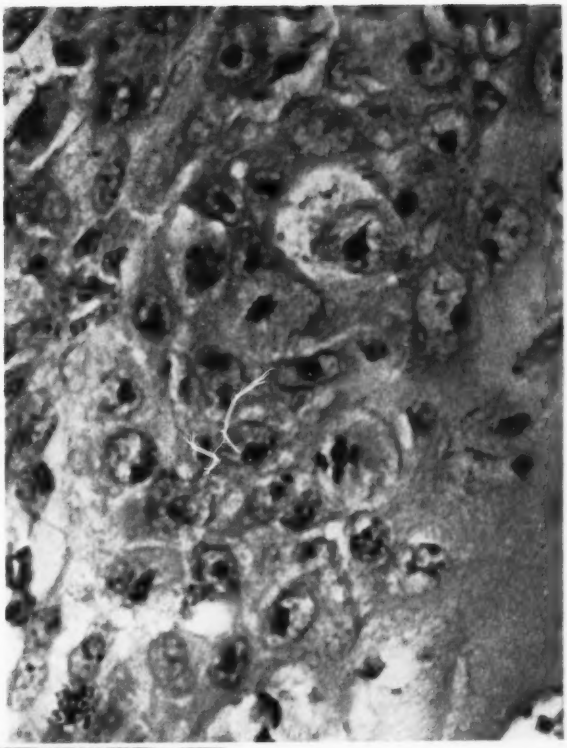


Fig. 8.—Atypical mitotic cells are present in these tumors. Hematoxylin and eosin; × 800.

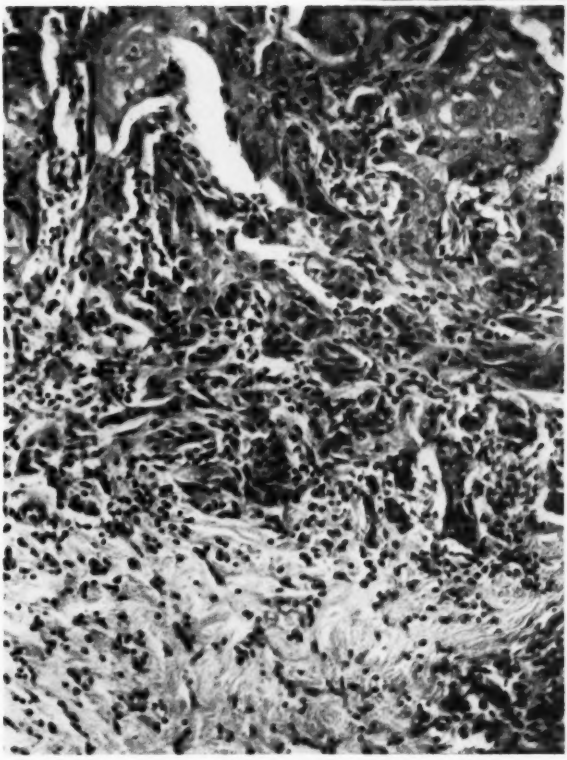


Fig. 9.—The periphery of these tumors is usually infiltrated with lymphocytes and leukocytes. Hematoxylin and eosin; × 170.

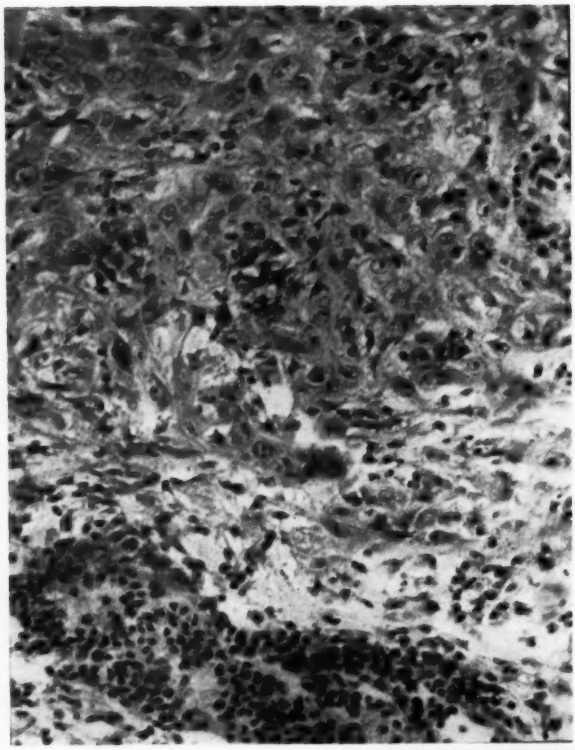


Fig. 10.—Many lymphocytes usually are present about the periphery of these lesions. Hematoxylin and eosin; × 340.

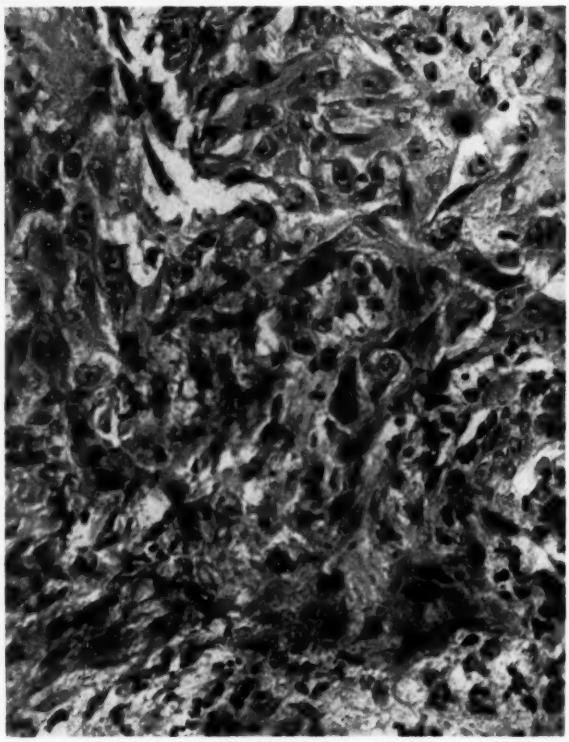


Fig. 11.—The nuclei of the squamous cells at the periphery of these regressing lesions are pyknotic. Subsequently, these cells atrophy and ultimately completely disappear. Hematoxylin and eosin; × 340.

and macrophages are around the epithelium in abundance. Degenerative cytologic epithelial changes are uniformly present and distinctive . . . . Mitoses are abundant in the hyperplastic epithelium and abnormal mitotic figures with chromosomal fragmentation and dispersion, usually outnumber the normal mitoses . . . . In the adjacent dermis, detached epithelial cells heavily infiltrated with leucocytes are found in keratoacanthoma.

The similarity of this lesion induced with methylcholanthrene in the skin of the chicken and the description of keratoacanthoma, as given by McNulty and Sommers,[16] is obvious. It is my opinion, and the opinion of others who have studied this lesion in the skin of chickens, that it is histologically a low-grade malignant epithelial tumor. However, since it regresses and does not metastasize, it has been described as a "squamous-cell carcinomatoid tumor," [21] although originally we reported it as a "squamous-cell carcinoma." [20] The problems in the differentiation of keratoacanthoma, squamous-cell carcinoma, and pseudoepitheliomatous hyperplasia are readily appreciated and have been discussed frequently.

The most interesting features about keratoacanthoma in man and the carcinomatoid tumors in chickens induced by methylcholanthrene are their histologic resemblance to squamous-cell carcinomas and their spontaneous regression. An increasing number of malignant tumors that regress spontaneously is being found in man and animals.[23-27] Little is known, however, as to the mechanism of regression. Haaland [28] suggested that a change must occur within the tumor cell to explain this phenomenon. Huggins [29] has emphasized the role of hormones in the regression of certain neoplasms. Cowdry,[30] in discussing the problems of "unexplained disappearance and alterations in the malignancy of cancer cells," suggests that "spontaneous modifications in the volume, or growth, of a cancer could result from many variables both of the malignant cells and of the stroma." Experimentally induced hemangiomas spontaneously regress as a result of a mechanical obstruction that occurs within the vascular channels. With the progressive decrease in blood flow through the vascular channels, tissue anoxia may become the significant factor in the mechanism of this spontaneous regression.[31]

The observation that the degree of cellular degeneration is more marked in the cells at the periphery of the chicken tumor induced by methylcholanthrene would suggest that some cellular injurious factor reaches these cells by way of the tissue fluid. Antibodies formed elsewhere in the body, reacting with the antigen represented by the proliferated epithelial cells, could account for this degeneration of the tumor cells. The degeneration might be expected to begin at the periphery of the lesion. In support of this hypothesis are the observations of Pollard and Bussell,[32,33] who found an inhibition of growth of methylcholanthrene-induced tumor tissue when the transplants were grown in the presence of splenic tissue obtained from mice previously inoculated subcutaneously with methylcholanthrene. This tumor-destructive effect could not be demonstrated with "normal" spleens or with the spleens from mice supplying the tumor tissue. Furthermore, this reaction could not be induced with spleens from mice treated with other carcinogens; too, when a carcinogenically induced transmissible tumor involuted, the recovered host was refractory to reinoculation with the same tumor.

It would seem of interest to observe persons with keratoacanthomas closely from an immunological standpoint. A regression of these lesions may be related in some way to an immune process. In view of the histological similarity of the keratoacanthoma and a low-grade squamous-cell carcinoma, it might be that some immune process occurs in the person to account for the regression of the former lesion. A history referable to the resistance to bacterial infections, allergic manifestations, and serologic and chemical observations on the serum might contribute something to the mechanism of regression of neoplasms, a process that rarely occurs in man but does occur frequently in laboratory animals.

Ghadially,[19] in 1958, pointed out the similarity of lesions produced by 9:10-dimethyl-1:2-benzanthracene in the skin of the rabbit to keratoacanthomas in man. The paper by Ghadially [19] came to my attention after this manuscript had been prepared. It is of considerable interest, however, to observe the close similarity of the history and the morphology of these lesions in man and the rabbit. Too, the lesions in the chicken are very similar to those in the rabbit. Keratoacanthomas, according to Ghadially,[19] appear to start by hyperplasia of the hair follicles and metaplasia of the sebaceous glands. Fragments of hair shafts often persist; this lends support to the suggestion that these lesions arise from hair follicles and not as downgrowths from the epidermis.[19] The fact that multiple lesions histologically similar to keratoacanthomas can be produced in the rabbit with carcinogens suggests the possibility that cases of multiple self-healing carcinomas may be no more than multiple keratoacanthomas arising in a genetically susceptible group of persons exposed perhaps to an undetected carcinogenic stimulus.[19]

Summary

A squamous-cell tumor occurs in the skin of chickens after the local application of methylcholanthrene. This tumor is characterized by a crater in which there is a large amount of keratin and leukocytes. Lymphocytes, histocytes, and leukocytes are present at the periphery of the growth. The tumor spontaneously regresses. The similarity of this squamous-cell tumor in the chicken to the keratoacanthoma in man is discussed.

University of Texas Medical Branch.

REFERENCES

1. Smith, J. F.: A Case of Multiple Primary Squamous-Celled Carcinomata of the Skin in a Young Man with Spontaneous Healing, Brit. J. Dermat. 46:267-272 (June) 1934.

2. Ereaux, L. P.: Schopflocher, P., and Fournier, C. J.: Keratoacanthoma, A. M. A. Arch. Dermat. 71:73-83 (Jan.) 1955.

3. Pegum, J. S.: Familial Primary Self-Healing Squamous Epitheliomata of the Skin (Ferguson Smith), Proc. Roy. Soc. Med. 47:403 (June) 1954.

4. Binkley, G. W.: Keratoacanthoma (Molluscum Sebaceum), A. M. A. Arch. Dermat. 71:66-72 (Jan.) 1955.

5. Beare, J. M.: Molluscum Sebaceum, Brit. J. Surg. 41:167-172 (Sept.) 1953.

6. MacCormac, H., and Scarff, R. W.: Molluscum Sebaceum, Brit. J. Dermat. 48:624-626 (Dec.) 1936.

7. Whittle, C. H., and Lyell, A.: Molluscum Sebaceum (Keratoacanthoma, Benign Epithelioma), Brit. J. Dermat. 64:424-425 (Nov.) 1952.

8. Levy, E. J.; Cahn, M. M.; Shaffer, B., and Beerman, H.: Keratoacanthoma, J. A. M. A. 155: 562-564 (June) 1954.

9. Bowman, H. E., and Pinkus, H.: Keratoacanthoma (Molluscum Sebaceum), A. M. A. Arch. Path. 60:19-25 (July) 1955.

10. Smith, J. F.: Multiple Primary Self-Healing Squamous Epithelioma of the Skin, Brit. J. Dermat. 60:315-318 (Oct.) 1948.

11. Currie, A. R., and Smith, J. F.: Multiple Primary Spontaneous-Healing Squamous-Cell Carcinomata of the Skin, J. Path. & Bact. 64:827-839 (Oct.) 1952.

12. Marshall, J., and Findlay, G. H.: Multiple Primary Self-Healing Squamous Epithelioma of the Skin (Ferguson Smith) and Its Relationship to Molluscum Sebaceum, South African M. J. 27:1000-1005 (Nov.) 1953.

13. Witten, V. H., and Zak, F. G.: Multiple, Primary, Self-Healing Prickle-Cell Epithelioma of the Skin, Cancer 5:539-550 (May) 1952.

14. Grzybowski, M.: A Case of Peculiar Generalized Epithelial Tumors of the Skin, Brit. J. Dermat. 62:310-313 (July-Aug.) 1950.

15. Epstein, N. N.; Biskind, G. R., and Pollack, R. S.: Multiple Primary Self-Healing Squamous-Cell "Epitheliomas" of the Skin, A. M. A. Arch. Dermat. 75:210-223 (Feb.) 1957.

16. McNulty, J. F., and Sommers, S. C.: Keratoacanthoma as a Surgical Pathologic Entity, Surg. Gynec. & Obst. 104:663-668 (June) 1957.

17. Sommerville, J., and Milne, J. A.: Familial Primary Self-Healing Squamous Epithelioma of Skin (Ferguson Smith Type), Brit. J. Dermat. 62:485-490, 1950.

18. Poth, D. O.: Tumor-like Keratoses: Report of a Case, Arch. Dermat. & Syph. 39:228-238 (Feb.) 1939.

19. Ghadially, F. N.: A Comparative Morphological Study of the Keratoacanthoma of Man and Similar Experimentally Produced Lesions in the Rabbit, J. Path. & Bact. 75:441-453 (April) 1958.

20. Rigdon, R. H., and Brashear, D.: Experimental Production of Squamous-Cell Carcinomas in the Skin of Chickens, Cancer Res. 14:629-631 (Oct.) 1954.

21. Rigdon, R. H., and Hooks, M. D.: A Consideration of the Mechanism by Which Squamous-Cell Carcinomatoid Tumors in the Chicken Spontaneously Regress, Cancer Res. 16: 246-250 (March) 1956.

22. Rigdon, R. H.: Spontaneous Regression of Tumors Produced by Methylcholanthrene in the Skin of Fowl, presented at the First Pan American Cancer Cytology Congress, Miami Beach, Fla., April 25-29, 1957.

23. Bartley, O., and Hultquist, G. T.: Spontaneous Regression of Hypernephromas, Acta path. & microbiol. scandinav. 27:448-460, 1950.

24. Beck, S.: Spontaneous Regression of Histologically Malignant Tumours Induced in Rabbits by 9:10-Dimethyl-1:2-Benzanthracene, Nature, London 156:238-239 (Aug. 25) 1945.

25. Park, W., and Lees, J. C.: Choriocarcinoma, A. M. A. Arch. Path. 49:73-104 (Jan.); 205-241 (Feb.) 1950.

26. Rigdon, R. H.: Spontaneous Regression of Neoplasms: An Experimental Study in the Duck, South. M. J. 47:303-310 (April) 1954.

27. Stewart, F. W.: Experiences in Spontaneous Regression of Neoplastic Diseases in Man, Texas Rep. Biol. & Med. 10:239-253 (Spring) 1952.

28. Haaland, M.: Spontaneous Tumors in Mice, 4th Scientific Report on the Investigations of the Imperial Cancer Research Fund, London, 1911, pp. 1-113.

29. Huggins, C.: Endocrine Substances in the Treatment of Cancers, J. A. M. A. 141:750-754 (Nov. 12) 1949.

30. Cowdry, E. V.: Cancer Cells, Philadelphia, W. B. Saunders Company, 1950, Chap. 19.

31. Rigdon, R. H.; Walker, J., and Teddlie, A. H.: Hemangiomas: An Experimental Study in the Duck, Cancer 9:1107-1115 (Nov.-Dec.) 1956.

32. Pollard, M., and Bussell, R.: Role of the Spleen in Resistance to Epithelial Tumors, Texas Rep. Biol. & Med. 11:48-57 (Spring) 1953.

33. Pollard, M., and Bussell, R. H.: An Antineoplastic Factor in Spleens of Mice Previously Inoculated with Methylcholanthrene, Proc. Soc. Exper. Biol. & Med. 83:671-673 (Aug.-Sept.) 1953.

Methoxsalen and Sun-Tanning

A Blind Study

OTTO C. STEGMAIER, M.D., Davenport, Iowa

Earlier observations by Fitzpatrick et al.[1] and others[2-6] suggested that methoxsalen, when taken internally and followed by exposure to sunlight, produced increased pigmentation and decreased burning of the skin. Controlled field trials in Arizona proved that pigmentation of the skin is augmented by the oral use of this drug.[1] However, the recent blind study by Daniels et al.[7] casts doubts on the effectiveness of this drug when taken in a dosage of 10 mg. The results of present investigation, which compares the effects of a sugar placebo and 20 mg. methoxsalen, indicate that methoxsalen in this high dose augments the tanning response.

Experimental Method

Identical-appearing tablets of methoxsalen* (10 mg.) and a lactose sugar placebo were issued under code numbers so that neither the physician nor the patient knew which preparation the patient received. Subjects consisted of patients and volunteers, who were directed to take two tablets of the medication (20 mg.) two hours before exposure to the sun during the months of April and May. The amount of skin exposed varied from minimal exposures of the face and arms to total-body irradiation, while the frequency of exposures varied from once a week to five times a week. The subjects were advised to increase their exposure time in small increments.

Thirty-nine of the subjects had red or blonde hair, blue eyes, and fair skin, while the remainder had brown or black hair and moderately fair skin.

After completion of a minimum of one bottle (30 tablets) of either the placebo or the methoxsalen, the subjects were questioned to see if they had observed an increased tan or a decreased burn in comparison with past experiences without drugs.

Submitted for publication August 8, 1958.

*Methoxsalen (Meloxine) and placebos were supplied by Harold A. Tucker, M.D. of The Upjohn Company, Kalamazoo, Mich.

TABLE 1.—*Effect of Methoxsalen on Sun-Tanning* *

	Methoxsalen	Placebo	Total
Tans more	19	4	23
No change	9	12	21
Total	28	16	44

* $\chi^2 = 5.87$. Significant difference to 98% confidence limit. Not significant at 99% confidence limit.

Results

Tables 1 and 2 summarize the results. Five subjects could not complete the study. Nineteen of the twenty-eight subjects on the active drug indicated that tanning or pigmentation was more intense than in previous years. Four of the sixteen subjects on the placebo also indicated they had tanned more. The differences are statistically significant to the 98% confidence limit.

The patients' evaluation to decreased burning of the skin was not as significant. Fifteen of twenty-seven on the active medication indicated that there was less burning, while four of eighteen on the placebo also thought they burned less. The differences are statistically significant to the 90% confidence limit.

TABLE 2.—*Effect of Methoxsalen on Sunburning* *

	Methoxsalen	Placebo	Total
Burns less	15	4	19
No change	12	14	26
Total	27	18	45

* $\chi^2 = 3.64$. Significant difference to 90% confidence limit. Not significant at 95% confidence limit.

Comment

Experimental work in animals and humans with mercury-vapor lamps [8,9] and black-light fluorescent lamps [6] indicate that long-wave ultraviolet waves (above 3,200 A) are probably the principal activating waves of the furocoumarins. Since the sun in April and May contains a higher proportion of these rays than the midsummer sun, the differences between the results obtained from this experiment and those of Daniels et al. may be reconciled. Probably the most likely explanation of the differences resulting from these two experiments is the difference in dosage employed. Daniels' group compared the results of largely 10 mg. of methoxsalen, while in this experiment 20 mg. was administered.

Summary

Pre-solar-ingested methoxsalen when employed in sufficient dosage in comparison to a placebo will cause increased tanning (98% confidence level) and decreased burning of the skin (90% confidence level).

The University of Oregon Medical School, Division of Dermatology, did the statistical analysis.

609 First National Building.

REFERENCES

1. Fitzpatrick, T. B.; Hopkins, C. E.; Blickenstaff, D. D., and Swift, S.: Augmented Pigmentation and Other Respones of Normal Human Skin to Solar Radiation Following Oral Administration of 8-Methoxypsoralen, J. Invest. Dermat. 25:187 (Sept.) 1955.

2. Lerner, A. B.; Denton, C. R., and Fitzpatrick, T. B.: Clinical and Experimental Studies with 8-Methoxypsoralen in Vitiligo, J. Invest. Dermat. 20:299 (April) 1953.

3. Lerner, A. B.: Potentiation of Sun Tanning Through Ingestion of 8-Methoxypsoralen, J. Invest. Dermat. 25:1 (July) 1955.

4. Arnold, H. L., Jr.: Psoralens and Sun Tan: Augmentation of Skin Responses to Sunlight by Psoralen Derivatives, Hawaii M. J. 16:391, (March-April) 1957.

5. Elliot, J. A., Jr.: Clinical Experiences with Methoxsalen in Sun Tanning, J. Invest. Dermat., to be published.

6. Stegmaier, O. C.: The Use of 8-Methoxypsoralen in Sun Tanning, J. Invest. Dermat., to be published.

7. Daniels, F., Jr.; Hopkins, C. E., and Fitzpatrick, T. B.: Effects of Oral Methoxsalen (8-Methoxypsoralen) on Sunburn and Suntan, A. M. A. Arch. Dermat. 77:503-507 (May) 1958.

8. Pathak, M. A., and Fitzpatrick, T. B.: Relationship of Molecular Configuration to the Activity of Furocoumarin Which Increases the Cutaneous Responses Following Long Wave Ultra Violet Radiation, J. Invest. Dermat., to be published.

9. Griffin, A. C.; Hakim, R. E., and Knox, J. M.: Wave Length Effect upon the Erythematous and Carcenogenic Response in Psoralen Treated Mice, J. Invest. Dermat., to be published.

Relaxin (Releasin) Therapy in Diffuse Progressive Scleroderma

A Preliminary Report

JAMES A. EVANS, M.D., Boston

The results of all methods of treatment in 38 cases of diffuse progressive scleroderma were reported from this clinic in 1953.[1] Twenty-five of these patients had been subjected to extensive sympathectomy. The results of all forms of medical treatment, including steroid therapy, had been disappointing. A follow-up study ranging from 3 months to 11½ years was made, and we concluded that extensive sympathectomy gave the best palliative results, having an ameliorating influence in about 88% of patients. Improvement was noted chiefly in the skin areas of the face, yoke, upper arms, and legs and symptomatically on the esophagus and larynx. Sympathectomy from the first to the fifth thoracic segments is of value when the face, yoke, and arms are involved but not the esophagus. However, since the esophagus was involved in 45% of all our patients and in 65% of those with facial involvement and since the esophagus became involved in three patients after sympathectomy limited to the upper segments, we now advocate sympathectomy of the 1st to 12th thoracic segments, leaving a gap on one side supplying the greater splanchnic nerve. The gap is left to prevent a possibly incapacitating postural hypotension in a normotensive patient. Hands have not been benefited very much where the skin is close to the bone and where only a small amount of subcutaneous tissue is present. If the lower limbs are involved, the sympathectomy is carried down to the third or fourth lumbar segment.

Received for publication April 28, 1958.

Department of Internal Medicine, the Lahey Clinic.

In an attempt to help these unfortunate patients further, we have been using relaxin (Releasin)* intravenously, intramuscularly, and by rectal suppository. The purpose of this communication is to report our results after nearly two years of use of this pregnancy ovarian hormone on patients who have had sympathectomy. The hormone was administered to two patients before sympathectomy, to three immediately after sympathectomy, and to six patients three months to four years nine months after sympathectomy.

Relaxin is a polypeptide-like hormone which occurs most abundantly during pregnancy. Its actions were first observed in connection with normal changes in the pelvic ligaments during pregnancy in some species of animals. Similar changes were produced in the pubic symphysial ligament of estrogen-primed oophorectomized guinea pigs by injection of pregnant-rabbit serum or aqueous extracts of sow corpora lutea. Subsequent observations demonstrated that symphysial "relaxation" was associated with definite histologic and biochemical changes in the connective tissue of the pelvis.[2-5] The chemistry and biology of relaxin have been reviewed by Hisaw and Zarrow,[6] Frieden and Hisaw,[7] and Sher and Martin.[8] †

Boucek et al.[9] presented an excellent review of the known physiologic effect of relaxin "on the metabolism of the

* Supplied by the Warner-Chilcott Laboratories, Morris Plains, N. J.

† Personal communication by R. L. Kroc and B. G. Steimetz, of the Warner-Chilcott Laboratories.

fibroblasts, the appearance and number of the mast cells, the general appearance of the ground substance and the molecular structuring of the collagen fibres." They reported on 13 unsympathectomized patients with scleroderma, primed on estrogen, in whom the effects of the disease were ameliorated. They noted healing of digital ulceration and loosening of the skin.

Description of Cases

Of 11 sympathectomized patients treated with relaxin (Releasin), nine were females and two, males. Their ages ranged from 19 to 55 years at the time relaxin was started. All exhibited widespread scleroderma, which was especially severe in the hands and face, except in one case. All but one had Raynaud's phenomenon. Nine of the eleven patients had esophageal involvement, in two instances severe enough to require dilation, and one of these patients had a "carcinoma in situ." A third had very severe esophagitis in a tube-like esophagus.

Six patients had pulmonary scleroderma, in one of whom it was so severe that the patient had two attacks of pulmonary edema. Two patients had enlarged hearts and exhibited nonspecific electrocardiographic changes presumably due to scleroderma, since no hypertension or evidence of rheumatic heart disease was present. They were both asymptomatic with regard to cardiac symptoms. One had gastric scleroderma, and another patient who died probably had intestinal scleroderma. Four had laryngeal involvement and were hoarse.

Use of Diethylstilbestrol

All 11 patients were primed with diethylstilbestrol, 1 mg. daily, and this was continued throughout therapy. When menorrhagia occurred in four patients, diethylstilbestrol was discontinued until bleeding stopped and then resumed at a lower dosage. Temporary slight hypertrophy of the breasts developed in one male patient. This subsided although the dose of diethylstilbestrol was not altered.

Method of Relaxin Therapy

Duration of treatment has ranged from 7 to 23 months. Treatment was started in the hospital in seven cases with relaxin given intravenously for three to seven days in increasing doses from 2.5 mg. to 80 mg. in 5% dextrose and saline solution. After preliminary intravenous therapy the gel preparation was given intramuscularly in doses ranging from 30 mg. to 50 mg. two to seven times a week. According to the availability of material and soreness of the buttocks, the saline preparation was sometimes alternated with gel injections. Four patients have subsequently received rectal suppositories containing 40 mg., taken each night. Four ambulatory patients were started on intramuscular gel relaxin. All patients were first tested with 0.1 cc. of relaxin in saline solution intradermally to rule out allergy.

Complications of Relaxin Therapy

Local allergy to injections of relaxin in gel developed in two patients, but they continued to tolerate injections when two drops of hydrocortisone was added to the material. One patient had a fatal anaphylactoid reaction after intravenous injection of about 1 mg. of relaxin. She had been under constant treatment for 20 months, at first receiving intravenous doses up to 80 mg., then intramuscular injections up to two months before death, during which time she used rectal suppositories daily. This tragic occurrence should stand as a warning that any patient should be retested for sensitization if he is to receive intravenous therapy again after a course of relaxin by other routes.

The gel preparation caused great discomfort if given too low in the buttock; severe buttock soreness also occurred after a few weeks if the gel preparation were given daily. Four of these patients with sore buttocks are now taking relaxin in suppository form. Two patients were subsequently given relaxin in saline solution intramuscularly. In two patients who had postural hypotension as a result of sympathectomy,

relaxin seemed to exaggerate their sense of exhaustion when standing up, but this disappeared with temporary cessation of therapy.

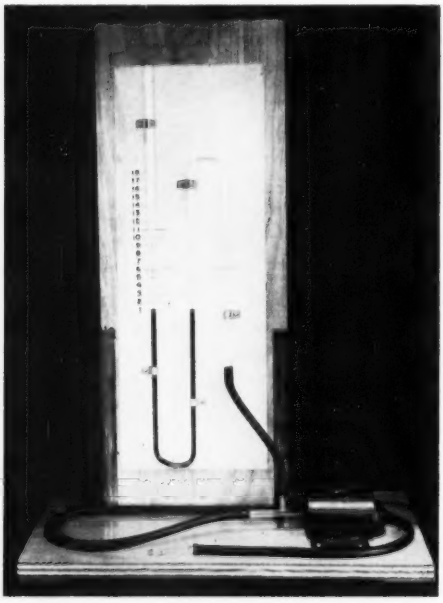
Effect of Relaxin When Given Before Sympathectomy

When the hormone was given before sympathectomy in two patients, one became progressively worse, and no notable improvement was observed after sympathectomy. This patient died of an anaphylactoid reaction. The second patient improved only slightly after three months' treatment. However, one month after sympathectomy the neck and thoracic skin loosened up well. Measure of skin resistance by a saline injection pressure gauge showed that relaxin therapy, continued by rectal suppositories of 40 mg. for 14 months, caused further loosening of the skin (Fig. 1 and Table 1). This patient was one of two males in our series, and his condition was unusual in several respects. He never had Raynaud's phenomenon. The onset was acute with arthralgia and fever. The involvement was *en cuirasse*, with severe scleroderma of the upper arms but not of the hands, face, or viscera. At first he was thought to have scleredema, and this impression was borne out by biopsy; however, two months later the findings after a second biopsy were typical of scleroderma.

TABLE 1.—*Saline Skin Resistance After Three Months of Relaxin Intramuscularly and by Rectal Suppository, and After Thoracic Sympathectomy Plus Fourteen Additional Months of Relaxin by Rectal Suppository, 40 Mg. Daily*

	Saline, Cm.			
	Right		Left	
	9/5/57	11/26/58	9/5/57	11/26/58
Dorsum of hand	65	30	100	35
Volar surface of forearm	110	60	100	60
Acromioclavicular joint	290	60	300	60
Anterior superior spine of ilium	200	65	--	70

Fig. 1.—Machine for measuring intradermal tissue pressure (designed by Sodeman and Burch [19]). Unfortunately, we did not have this valuable aid to study skin improvement objectively over the entire period of observation of our patients in this series.



Effect of Relaxin Given Months to Years After Sympathectomy

Six patients started courses of relaxin therapy long after sympathectomy, when improvement had seemed to reach a plateau. The skin areas showed definite further improvement in four of these cases. One patient exhibited decided improvement of the face and hands after sympathectomy alone before relaxin was started. In fact, he was able to resume piano practice again, being a professional pianist. However, the esophageal scleroderma and esophagitis remained a major problem after seven months of relaxin therapy. At this time he was rehospitalized for duodenal ileus brought on by severe postural hypotension, malnutrition, and development of mesenteric pedicle compression. Gastroenterostomy was performed. Intense intravenous relaxin therapy was then carried out for one week, the patient receiving 20, 40, 80, 80, and 80 mg., respectively, in dextrose daily. During

these five days he continued to be very depressed and vomited bile but not food. Swallowing was very difficult. A roentgenogram of the esophagus showed that it was still a narrow tube with minimal peristalsis. This patient had undergone a very extensive sympathectomy, from the 2d thoracic to the 4th lumbar on the left and the 1st through the 10th thoracic and the 2d and 3d lumbar on the right. The "gap" on the right side did not include the main branches to the greater splanchnic nerve, but these were omitted purposely in order to sympathectomize the badly involved esophagus more thoroughly. Since going home, the patient has continued to vomit. His skin improvement is attributed to sympathectomy and occurred before relaxin was given.‡ The sixth patient in this group died of an unknown cause.

Effect of Relaxin Given Immediately After Operation

Because we found that sympathectomy often resulted only in improvement to a certain plateau, and sometimes none, and since the esophagus proved to be a major problem in some cases even after sympathectomy, we decided to use relaxin immediately after operation. This policy was supported by a lack of any notable improvement in the two patients who had received relaxin before sympathectomy.

Of the three patients who were given relaxin immediately after sympathectomy, one received 50 mg. of gel three times a week for four months and reported she was very happy with the result and was back at work. The skin of the hands and arms had improved, and the Raynaud's phenomenon was gone. She could drive her car in cold weather without gloves. The trophic lesions on her fingers had healed. She had undergone bilateral sympathectomy of the 1st through the 10th thoracic segments. Roentgenograms revealed esophageal scleroderma, which was asymptomatic.

‡ This patient subsequently died from a ruptured esophagus.

In another of these three patients involvement of the arms, hands, and legs was extensive, with resistant ulcers over both malleoli of the left ankle. A bilateral lumbar sympathectomy was performed nine months previously, and relaxin therapy started at the same time. The first three doses consisted of 80 mg. intravenously; then 50 mg. of gel was given every second day for five and one-half months. Although unsympathectomized, the skin in the thoracic area, the forearms, yoke area, and face became much looser. The hands did not improve, and, although the lower extremities were sympathectomized, the leg ulcers were no better. The patient was, therefore, hospitalized and for one week received chloraquine, 500 mg. daily, without improvement. Relaxin was given intravenously, 80 mg. daily, together with chloraquine.§ She also was taking 1 mg. of diethylstilbestrol per day during this five and one-half month period. The ulcers appear to be improving.

The third patient in this group died four months after operation, during which time relaxin in saline solution, 20 mg. three times a week, had been given. She had had the disease only one year and exhibited pronounced scleroderma of the whole integument with pigmentation and edema of the legs. Scleroderma affected both the esophagus and lungs. Death was caused by anuria; the immediate cause was choking on scrambled eggs. She also had undergone a very extensive bilateral sympathectomy, from the first thoracic to the second lumbar, with a gap of the sixth, seventh, and eighth in order to preserve the splanchnic nerves. After two and one-half months of therapy, she wrote that "the skin seems so much more relaxed." However, her doctor wrote at the time of death that "her lower limbs were board-like and she could not walk the last four days."

§ Personal communication from Dr. Bayliss, who reported dramatic improvement in one patient with scleroderma of the hands on combined relaxin and chloraquine therapy.

Effect on Viscera

Esophagus.—Of nine patients with esophageal scleroderma demonstrated by barium swallow, eight had dysphagia. Difficulty in swallowing was improved in three, although the roentgenogram still showed involvement. In a fourth patient, the dysphagia disappeared entirely, and barium swallow no longer indicated the presence of disease. Four patients showed no signs of improvement, either symptomatically or on the roentgenogram of the esophagus, and in one patient the follow-up observation has been too short to tell what the outcome will be.

Lungs.—No follow-up chest roentgenograms have been taken as yet in patients with pulmonary scleroderma, except in one patient, who had two attacks of acute pulmonary edema. In this case the x-ray appearance of the lungs remained the same, but after 22 months of relaxin therapy paroxysmal dyspnea and cough have disappeared and exertional dyspnea is greatly improved. Both of the acute attacks were relieved by intensive intravenous therapy with doses up to 80 mg. of relaxin daily for 7 and 11 days, respectively. Objective improvement was also evident in the skin resistance test and vital capacity (Tables 2 and 3).

Larynx.—Hoarseness has become less severe in two of three patients with laryngeal involvement.

Heart.—No follow-up information is available at this time.

TABLE 2.—*Intradermal Tissue Pressures Before and After Administration of 350 Mg. of Relaxin Intravenously in Eleven Days* *

	Saline, Cm.			
	Right		Left	
	Before	After	Before	After
Dorsum of hand	140	100	140	44
Over midclavicle	80	34	80	34
Dorsum of foot	120	60	104	42
Over anterior superior spine of ilium	60	42	60	42

* Doses: 20, 20, 20, 20, 20, 20, 40, 40, 50, 50, 50, mg.

TABLE 3.—*Vital Capacity in Patient with Pulmonary Scleroderma and Acute Pulmonary Decompsensation Before and After Intensive Course of Relaxin Intravenously and Intramuscularly* *

Time, Sec.	Before, Cc.	After, Cc.
1	900	1,200
2	1,000	1,300
3	1,100	1,400

* 20-50 mg. for 3 days and 30 mg. daily for 6 days intravenously; then 40 mg. in gel intramuscularly every second day for next 5 wk.

Results on Leg Ulcers.—One 37-year-old woman who had had sclerodermatous ulcers on her legs since the age of 14 has shown dramatic improvement and healing (Fig. 2).

Another patient underwent thoracic sympathectomy for scleroderma of the face and yoke area. Ulcers developed over the shins in the unsympathectomized legs. Desultory use of relaxin gel intramuscularly did not bring about healing, and this patient objected to soreness in the buttocks. When she received rectal suppositories of relaxin (40 mg.) for three months, the ulcers healed (Fig. 3). The healing of leg ulcers by rectal suppositories in this case has been our principal supporting evidence that relaxin by the rectal route is effective.

A third patient with leg ulcers underwent a bilateral lumbar sympathectomy and received relaxin gel, 50 mg. every other day, for five and one-half months; intensive intravenous therapy was then given without healing. The leg ulcers showed but little improvement after treatment with suppositories of relaxin for two months, during which time she could not retain them. However, during the last two weeks she has retained them well and reports that the ulcers are slowly healing and have been less painful.

Pigmentation has faded in two patients, as noted in colored photographs, over the years. One of these patients is shown in Figure 4. Some of this effect is the result of sympathectomy, but further fading occurred after relaxin. The patient attests to the fact that this pigmental fading is real and not merely the result of photographic

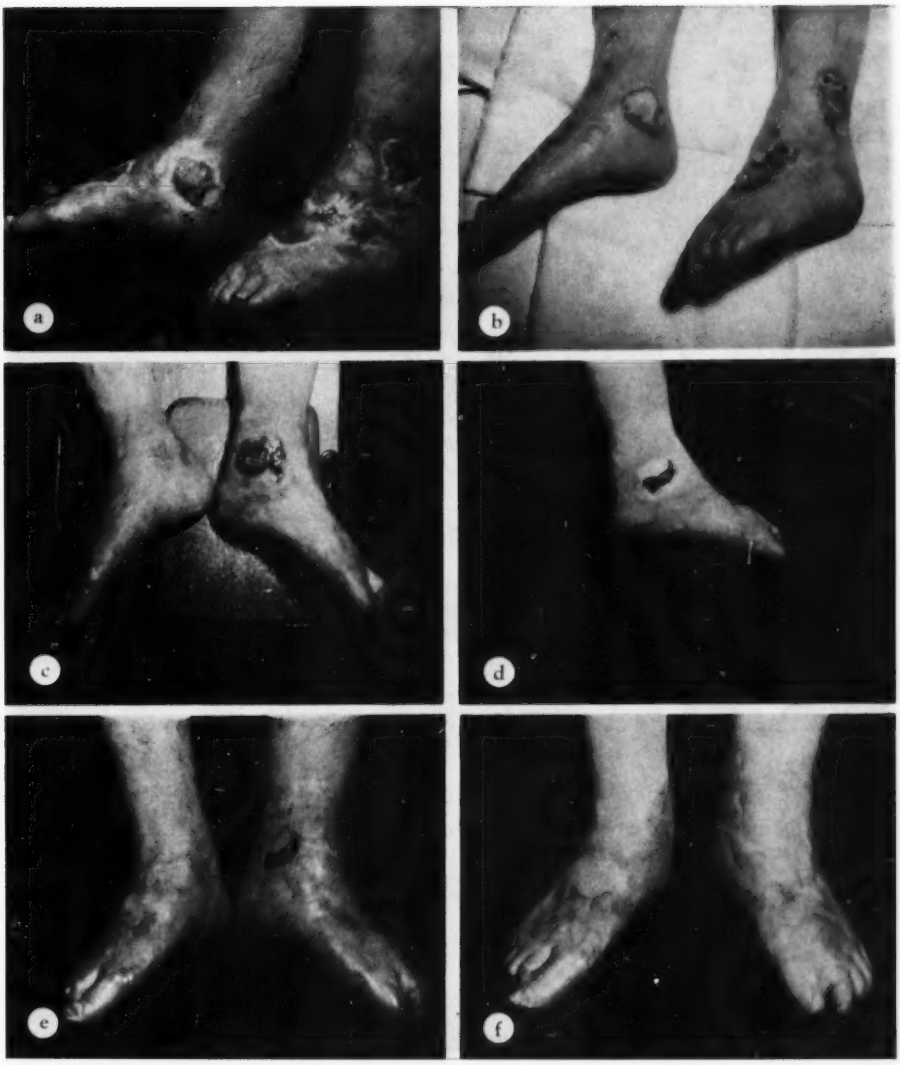


Fig. 2.—(a) April 22, 1953, before releasin treatment. These ulcers were present for 23 years. (b) June 12, 1953, after seven weeks of topical treatment before lumbar sympathectomy. (c) Oct. 28, 1955, two years four months after sympathectomy plus topical therapy. (d) March 6, 1956, only this one ulcer remained two years nine months after sympathectomy, before starting releasin on this date. (e) Ulcer beginning to heal after two months of intramuscular releasin therapy. (f) Feb. 20, 1957, ulcer healed after 11 months of intramuscular releasin therapy.

Fig. 3.—(a) Dec. 14, 1956. Thoracic sympathectomy April 16, 1956. Desultory treatment with intramuscular injections of saline and gel releasin (buttocks too sore) was given from July, 1956, to June, 1957. During this time ulcers developed on leg. (b) June 14, 1957, after seven months more of desultory therapy with releasin given intramuscularly one ulcer has healed. (c) Aug. 8, 1957, after two months of daily use of rectal suppositories of releasin, 40 mg. each, second ulcer has healed.

Fig. 4.—(a) May 3, 1951, one year after thoracic sympathectomy. Lumbar sympathectomy was performed two days after this picture. (b) October, 1957, after 20 months of releasin therapy and four years nine months after extensive sympathectomy. Note loss of pigmentation. (c) October, 1957, before releasin therapy she could abduct arms to 120 degrees. Hands have improved only slightly.

technique or darkening of the first colored print over the years.

Summary

The relaxin hormone obtained from the ovaries of pregnant sows (Releasin) helps to loosen the skin of sclerodermatous patients.

Sympathectomy combined with relaxin and diethylstilbestrol therapy brought greater flexibility of the skin in 8 of the 11 patients, being most effective in the face, neck, yoke, upper and lower arms, chest, abdomen, and legs. The hands showed a little improvement, such as healing of ulcers or erosions. However, finger mobility was rarely improved.

We have the impression that relaxin has a better effect in sympathectomized areas of the skin, because in two patients who had received relaxin before sympathectomy, the skin showed no definite improvement.

Of three patients who received relaxin immediately after sympathectomy, the skin of one was notably improved. The second patient showed improvement in the unsympathectomized facial, cervical, and arm skin but only slight improvement as yet in the sympathectomized leg area with an ulcer. The third patient died four months after treatment was started.

Relaxin has also led to further loosening of the skin in four of six patients. In these cases, the therapy was begun four months to four and three-fourths years after sympathectomy when improvement had reached a plateau.

One patient with severe pulmonary scleroderma was twice saved from acute pulmonary decompensation by vigorous therapy with relaxin given intravenously. Shoulder mobility improved spectacularly following the first episode. Notable improvement of the voice occurred in two instances, one patient being able to sing again.

In one patient, leg ulcers which had been present for 23 years and persisted after lumbar sympathectomy, finally healed on relaxin therapy. In a second patient with a leg ulcer who had undergone only a thoracic sympathectomy, the ulcer healed in two months on relaxin suppositories when desultory therapy with intramuscular injections had failed.

Barium swallow showed esophageal scleroderma in 9 of the 11 patients who had esophageal scleroderma; 8 of these patients had dysphagia. Improvement of dysphagia was notable in four patients, including two who had required dilation. Dysphagia did not improve in three instances. In the one patient who had asymptomatic scleroderma of the esophagus, roentgenograms still show evidence of esophageal disease. The observation period is too short for comment in the ninth patient. Eight of the nine patients with scleroderma of the esophagus demonstrated by x-ray examination still show evidence of the disease by barium swallow.

Three of the eleven patients in this study have died: one died of esophageal involvement; one with intestinal involvement died of unknown cause, and one died of an anaphylactoid reaction after intravenous injection of relaxin.

Lahey Clinic, 605 Commonwealth Ave. (15).

REFERENCES

1. Evans, J. A., Rubitsky, H. J., and Perry, A. W.: Treatment of Diffuse Progressive Scleroderma, J. A. M. A. 151:891-899 (March 14) 1953.

2. Catchpole, H. R.; Joseph, N. R., and Engel, M. B.: Action of Relaxin on Pubic Symphysis of Guinea-Pig, Studied Electrometrically, J. Endocrinol. 8:377-385 (Oct.) 1952.

3. Hall, K.: Changes in Bone and Cartilage of Symphysis Pubis of Mouse During Pregnancy and After Parturition, as Revealed by Metachromatic Staining and Periodic Acid-Schiff Technique, J. Endocrinol. 11:210-222 (Aug.) 1954.

4. Crelin, E. S.: Mitosis in Adult Cartilage, Science 125:650 (April 5) 1957.

5. Zarrow, M. X.; Neher, G. M.; Sikes, D.; Brennan, D. M., and Bullard, J. F.: Dilatation of the Uterine Cervix of the Sow Following Treatment with Relaxin, Am. J. Obst. 72:260-264 (Aug.) 1956.

6. Hisaw, F. L., and Zarrow, M. X.: Physiology of Relaxin, in Vitamins and Hormones, edited by

R. S. Harris and K. V. Thiman, New York, Academic Press, Inc., 1950, Vol. 8, p. 151.

7. Frieden, E. H., and Hisaw, F. L.: Biochemistry of Relaxin, in Recent Progress in Hormone Research, edited by H. Pincus, New York, Academic Press, Inc., 1953, Vol. 8, p. 333.

8. Sher, I. H., and Martin, G. J.: Relaxin, a Review, Exper. Med. & Surg. 14:89-98, 1956.

9. Boucek, R. J.; Nobel, N. L.; Casten, G. G.; Elden, H. R., and Kao K.-Y. T.: Effect of Releasin on Connective Tissue, presented before the Academy of Dermatology and Syphilis, Chicago, Dec. 13, 1956.

10. Sodeman, W. A., and Burch, G. E.: Tissue Pressure: An Objective Method of Following Skin Changes in Scleroderma, Am. Heart J. 17: 21-26 (Jan.) 1939.

Observations on Radiation Exposure in Dermatologic X-Ray Therapy

HERBERT S. ALDEN, M.D.; H. STEPHEN WEENS, M.D., and HARRY D. YOUMANS, B.S., Atlanta

Although for 50 years, since men began to use x-rays in the diagnosis and treatment of disease, the medical profession has been concerned with the safety of the patient in radiation procedures, it was not until recently that the extent of the radiation hazard became apparent to us all—physician, atomic scientist, and the public alike. This was in part due to a previous lack of accurate mensurating devices and a lack of basic standards. But, strangely enough, it was the alarm produced among the geneticists by the explosion of the thermonuclear bomb that drew attention to the radiation exposures which have long occurred in the practice of medicine.

In 1956, two groups of radiation specialists, atomic scientists and geneticists, assessed the radiation dangers to the general public, particularly from the explosion and manufacture of the atomic and hydrogen bombs. The reports of these men on the biologic effects and possible hazards of ionizing radiation were published in the United States by the National Academy of Scientists [1] and in England by the Medical Research Council of Great Britain.[2]

These reports, especially that of the Medical Research Council of Great Britain, if read carefully, show the distinguished authors to be fully conscious of the paucity of accurate data on which to base final conclusions and of the many unknowns and uncertainties in producing radiation protective standards or even coming by more than an "educated guess" for a "minimal permissible dose" of x-radiation for the general public. As for the genetic effects of radiation to the gonads and its possible production of dangerous mutations, the report read as follows:

"Nowhere in this report have we been more conscious of the difficulties of the task and of limitation of knowledge at our disposal than in considering the genetic effects of radiation. The established scanty evidence in this field provides but an insecure basis on which to frame answers to the many important questions now being asked."

A geneticist, H. J. Muller, whose experiments with mutations in the fruit fly produced by x-rays and whose writings on the subject have often been reported out of context,[3,4] seems to have had much to do with the alarm over harmful mutations of human genes when exposed to atomic radiation. In 1955, Muller [5] has already become concerned over ". . . the wide circulation of some statements by certain prominent publicists, that the bombings of Nagasaki and Hiroshima have left the descendant population unharmed or even improved . . ." and of others of the same ilk ". . . urging an end to all nuclear tests on the ground that they have already seriously undermined the genetic basis of all men." He writes that "both of these contrary claims are so far from the truth that they can only be interpreted as special pleadings dictated by an ulterior motive." But he adds that physi-

Submitted for publication July 29, 1958.

This study was aided by Grant No. C-3109 United States Public Health Service.

Read before the 78th Annual Meeting of The American Dermatological Association, Inc., Sun Valley, Idaho, June 7, 1958.

From the Department of Dermatology and the Departments of Radiology of the Emory University School of Medicine, Emory University, Ga.

cians often prefer ignorance of the matter to controversy and reform.

But does this mean, as some have implied,[6,8] denunciation of all atomic testing and of the continued use of x-rays in medicine? Not at all. The genetics committee of the National Academy of Science[1] "recommends the *general public* (not an individual) of the United States be protected, by whatever controls may prove necessary, from receiving a total reproductive life-time dose (from conception to age 30) of more than 10 Roentgens of man-made radiation to the reproductive cells." This, mind you, refers to *whole-body radiation.* They further recommend, "medical authorities of this country should initiate a vigorous movement to reduce the radiation exposure from x-rays to the lowest limit consistent with medical necessity; and in particular that they take steps to assure that proper safeguards always be taken to minimize the radiation dose to the reproductive cells." After assessing the hypotheses and the meager reports of possible genetic damage in man from radiologic procedures, the report to the Medical Research Council of Great Britain[2] concludes: ". . . if a relatively small group of prospective parents receive a doubling dose (range of 30-80 Roentgens) of radiation, no noticeable effects will be produced either on their immediate offspring or their descendants. For levels of radiation up to the doubling dose or even some way beyond, the genetic effects are only appreciable when received over the population as a whole and need cause no alarm to the individual on his own account." The reporters add that there is little or no information on the effects of the less penetrating rays used in therapeutic x-radiation, and it is not possible to state a figure for the dose to the gonads from this source.

In general, irrational fever and fears have been expressed by the press and in public statements and letters from leaders in the political and atomic fields, which show the deep concern for the moral involvement and guilt, associated with an aura of mystery, in the uninhibited use of atomic energy.

With this mixture of fear, force, and fraud some immature and unwise public statements have produced much exaggerated concern among the general public.[7,8] The medical profession has by no means been immune to these occurrences. In 1957, nearly every widely read medical journal contained excerpts from one or more of the reports referred to above, often coupled with editorials[9-13] warning of dire things to come because of uninhibited use of x-rays for the treatment of nonmalignant disease. The roentgenologists and the dermatologists have shared alike in these criticisms of past and present sins. But there are some calmer voices from Crow,[6] Neel,[15] Taylor,[14] and Teller.[28]

While the basic radiation standard, the "maximal permissible dose" for general occupational and public exposure, is no doubt accurate, a better and more realistic standard is needed as a guide for the medical profession as a whole. There is an obvious need for a better perspective in weighing the objectives. The physicians' contribution must be a desire to formulate a sort of philosophy of radiation protection, as well as to help in the development of radiation protective standards. But, since there are many uncertainties, many assumptions, and such frequent changes, we, therefore, must think in terms of protection goals rather than protective standards.[14,15] Even the goal is difficult of definition. For instance we must abandon the term "tolerance dose." It is a complete misnomer, since any amount of radiation is harmful. We must forget the "erythema dose" as a measurement for dermatologic therapy, since more modern measuring devices show that it may vary from 270 r to 1,000 r over a range from 100 to 1,000 kv. Since the 1930's, x-ray dosage has steadily been reduced. In 1934, the permissible dose was calculated at 0.2 of an erythema dose per day, and, in 1936, 0.1 of an erythema dose or 50 to

100 r; in 1948, it was 36 r, and, since 1948, it has been 15 r or less. While the permissible dose appears to have been reduced numerically, it is in fact probably not reduced biologically. But there is no single record in which such exposure produced detectable injury.[14,15]

It is important here to understand clearly that these dose figures and the figures given for the maximal permissible dose refer to whole body radiation and are not in reference to localized body exposure as used in good dermatologic procedure. It has been clearly pointed out by Crossland[16] that there has been much neglect among geneticists, atomic scientists, and medical men in not stressing this fact to both the general and the medical public.

It is in the light of these reports and these facts, if indeed they be facts, that we have in a small way made an attempt to measure the quantity of x-rays occurring at or near the gonads in patients receiving routine dermatologic therapy.

Laughlin, Meurk, Pullman, and Sherman[17] have very adequately summarized the estimates and measurements of gonadal dose that occurs in many radiologic techniques. They find that it is not realistic to produce a simple list of diagnostic procedures, each with its own specific and single value of associated gonad dose. Even if all the inherent variations of procedure (the kilovoltage, the milliamperage, distance, and tilt of tube or patient) among roentgenologists were known, the resultant estimate would still be only approximate. As would be expected, the closer the exposure to the pelvis the higher was the gonad dose. In the production of chest films using a kilovoltage of a 100 or less and a milliamperage of 5 or less (which approximates dermatological dosage) the average gonadal dose was 1 mr or less except in fluoroscopy when values rose to 3 mr. With more adequate lead shielding, on a phantom, Laughlin was able to show a reduction of this small exposure by 80% to 90%.

Chamberlin[18] presented data before the National Research Council on the approximate radiation received by the gonads from a single conventional x-ray film of the chest as of the order 0.25 mr and for a regular photofluorograph as of the order of 5.0 mr. Perkins estimates that this is 1/200th of the total dose received. It would then take 2,000 of such chest films during the first 30 years of life to use up the entire 10 r of gonadal radiation allowed by the permissible dose.

Many fewer experimental measurements and estimates of gonadal dosage from the use of superficial localized x-ray therapy as used by the dermatologist have been done. So there is a need of more studies among dermatologists in the manner so ably begun by Witten, Sulzberger, and Stewart.[19-21] Since dermatologists generally in the past 20 years have developed and abide by a standard of x-ray dosage both qualitative and quantitative,[22] such measurements should be considered as a more accurate estimate of the genetically significant dose to the gonads and, therefore, should not be subject to the wide variations inherent in the multiple techniques of the roentgenologist.

Among the first to produce such experimental evidence of gonadal dosage were Callaway, Moseley, and Barefoot,[23] who, in 1948, reported on the scattered radiation occurring at the testicle as measured by a Victoreen Roentgen Meter. They used a standard x-ray tube with a half-value layer of 0.35 mm. of aluminum, 85 kv., 3 ma., and tube distance of 25.4 cm. (10 in.), which produced a measured dose of 100 r per minute. Repeated calculations with a Victoreen Roentgen Meter showed that under these conditions each 100 r directed to the face of the phantom dummy resulted in an intensity of 34 mr (0.034 r) of scattered irradiation, measured in air at 75 cm. (30 in.) from the center of the x-ray beam. They conclude: "Since the average patient receiving roentgen ray therapy to the face received not more than sixteen treatments

of 100 r to each side of the face, a total of thirty-two exposures might be hypothecated. Assuming that the maximum of thirty-two exposures might be used in a given person, only 1.088 r (1,008 mr) would be expected to reach the scrotal area during the entire series of thirty-two treatments." We might add that this dose would occur over a period of 16 weeks. Their interest, however, was in the amount to sterilize or suppress spermatogenesis, not in the genetically significant dose of radiation.

Purser and Grist [24] undertook to obtain a rough estimate of the population genetic dose for radiotherapy by a sample survey of hospital procedures in the Copenhagen area, in 1957. But they included all radiotherapy, in which there were no fixed set of standards and no systematic direct measurements. They reported that gonad doses received from superficial skin therapy in the 30 to 60 kv. range (no record of other factors) were so low that a sample series of measurements was insufficient to establish the dose. They mention that badly shielded, usually antiquated, apparatus gave much higher gonad doses. But they conclude: "Even when taking into account the inaccuracies inherent in our methods we consider the contribution of radio-therapy to the genetically significant 'man-made' radiation is small enough to be negligible compared with diagnostic radiology."

Impelled by the same concern, which later prompted us to measure the gonadal dose, Witten, Sulzberger, and Stewart [19-21] early in 1957 reported a series of very careful and well-controlled studies on the quantity of radiation reaching the gonads in dermatologic therapy. We have been unable to discover any earlier or better series of direct systematic measurements during superficial skin treatment than that contained in these reports, and repetition of these measurements by others would seem desirable.

These authors rightly emphasize the importance of stating all the factors which may enter into the production of scattered radiation, in order to arrive at a reasonable estimate of that amount occurring at the gonadal area. They used two x-ray machines with an oil-cooled, glass-window x-ray tube mounted in a metal housing. One unit utilized a sturdy wooden table; the other, a steel-enclosed cabinet type table. Both machines delivered unfiltered radiation, with a half-value layer of 0.9 mm. of aluminum, operated at 90 to 114 kv. and 74 ma. The target-skin distance was 10 in. and the irradiated field no greater than 12 in. With use of one and sometimes two Keleket dosimeter readings in a calibrated scale from 0 to 200 mr placed in the genitocrural fold in males and under the back in females the quantity of radiation was measured in various positions. In the treatment of acne on the face in the prone position the dosimeter readings varied from 2 to 150 mr in a range of dose from 85 to 340 r. In the treatment of the hands in the sitting position the dosimeter readings varied from 0.0 to 200 mr in a dose range from 85 to 240 r. These wide variations in readings are very real and are dependent upon many factors, such as distance from x-ray tube to dosimeter (size and length of the patient), the placing of patient, and methods of shielding. Add to this the inherent variation in dosimeter sensitivity at such low rates of irradiation. These figures were closely approximated by many such "treatments" on a phantom dummy.*

Employing similar x-ray equipment, we have arrived at measurements of x-rays at or near the gonads that closely approximate those of Witten, Sulzberger, and Stewart.[19]

Equipment and Methods

Two x-ray machines were used in these observations. One was a Keleket model with an extension arm holding an air-cooled, metal-enclosed, Machlett x-ray tube above the patient and with a wooden treatment table with no metal attachments. The other, a standard Universal treatment x-ray machine and table, with a self-rectifying tube enclosed

* Such a short review of this series of papers is unfair to the authors. It is hoped that all interested in this subject will see fit to read these articles in their entirety.

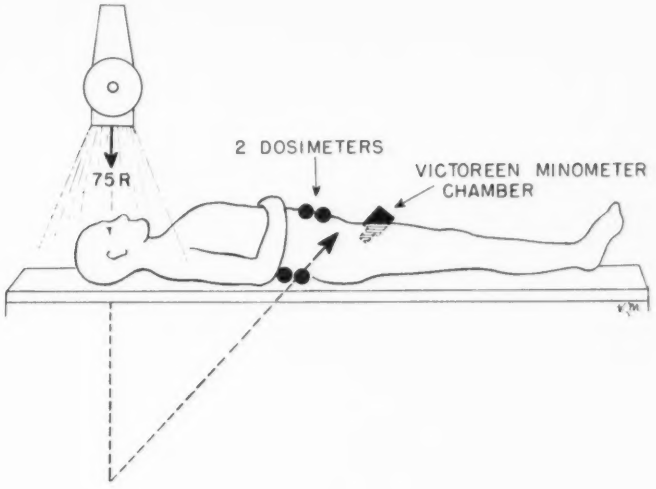


Fig. 1.—Method of measurement of radiation.

in a metal housing, attached to a stationary metal arm and upright. The table was metal, excepting the wooden top covered with a leatherette cushion. There was no equipment under either table.

Just prior to these observations both machines had been accurately calibrated and set to deliver x-ray as follows:

(1) Keleket and Machlett tube: HVL 0.75 mm. of aluminum at 86 kv., 5 ma. and TSD of 18.4 cm. (7.36 in.) to deliver 230 r per minute measured in air.

(2) Universal machine and tube: HVL 0.35 mm. of aluminum at 80 kv., 5 ma., and TSD of 24.4 cm. (9.76 in.) to deliver 140 r per minute measured in air.

A Victoreen Minometer Chamber of 10 mr capacity and Landsverk Dosimeters reading from 0.0 to 0.200 r and from 0.0 to 2 r were used in these experiments. All were calibrated against a Victoreen Condenser R-Meter.

With the patient lying prone on the table or sitting at the table, one finger type dosimeter was placed on each side of the lower abdomen and one in each lumbosacral area and the larger Victoreen Minometer Chamber was placed between the legs at the scrotum or perineal area (Figs. 1 and 2). Conventional shielding of the chest, scalp, and arms with lead rubber was done.

A total of 52 observations on 27 patients were performed. In one group of acne patients treatment was given to the face only, with no cone used; in another group of acne patients treatment was given to the chest, back, and face, with no cone used, and both types were treated with an 8 in. diameter copper cone; one group of patients was treated for hand eruptions, sitting at the table with and without cone. In addition, three patients were treated with perianal or groin eruptions and three patients were treated with small cones for epithelioma or verruca.

The amount of x-ray in milliroentgens as registered at these sites are reported as average readings of all patients so treated (Fig. 1 and Table 1).

Small changes in technique, such as tilt of the tube, movement and variations in lead shielding, height and weight of patient, and even size of the breast caused the readings to vary, and in addition there is an inherent variation factor of 35% to 40% in the dosimeters at the high and low kilovoltages. In addition, it is well known that there is some inherent leakage in all x-ray tubes (more in antiquated or poor equipment)[24] and it has been shown that 3 mm. of iron even more than lead is a poor scatterer of x-rays in the vicinity of the tube.[25] Some or all of these factors may account for the wide variation in the dosimeter readings in such observations as made by Witten et al. and by us. However, distance from the tube, direction of the ray, and density of the body seem to be the most important factors.

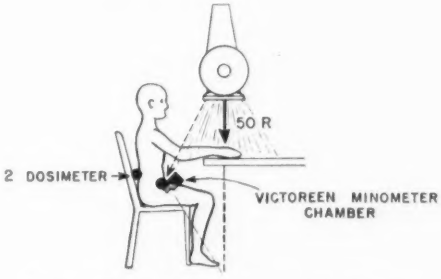


Fig. 2.—Method of measurement of radiation.

TABLE 1.—*Quantity of Radiation Reaching the Groin, Abdomen, and Sacral Regions in Routine X-Ray Treatment of the Skin* *

Total Dose Treatment, r (mr)	Skin Areas Irradiated	Distance from Tube to Pubis, In.	Cone Used	Lead Shield	Average Recorded Dose, mr		
					Groin	Abdomen	Sacrum
200 (200,000)	Sides & front of face	Average 21.6	None	Conventional	10.3	10.7	2.5
200 (200,000)	Sides & front of face	Average 21.6	Copper 8 in. diameter	Conventional	0.0	5.2	2.0
425 (425,000)	Sides & front of face, chest, & back	Average 21.6	None	Conventional	9.0	79.0	22.0
425 (425,000)	Sides & front of face, chest, & back	Average 21.6	Copper 8 in. diameter	Conventional	5.8	50.4	4.95
425 (425,000)	Sides & front of face, chest, & back	Average 21.6	None	Conventional & lead rubber abdomen	7.0	15.0	5.0

* Factors used: Machlett tube—HVL 0.75 Al., 85 kv., 5 ma., 8 in. TSD (18.4 cm.);
Universal tube—HVL 0.35 Al., 80 kv., 5 ma., 10 in. TSD (24.4 cm.);
Landsverk dosimeters—range of 0-0.2 r., 0-2.0 r;
Victoreen minometer chamber—range of 0-10 mr.

As would be expected, the more radiation used on the face or chest, and the closer the exposure to the pelvis, the greater was the dosimeter reading. But in the treatment of acne as shown in Table 1 when using a total dose of 200 r to the face only (75 r to each side and 50 r to the front), with no cone, and conventional lead shielding, we got average readings of 10 mr to the abdomen and groin, and 2.5 mr in the sacral region. When we used an 8 in. diameter copper cone with the same treatment factors, no readings could be had in the groin, only 5 mr at the abdomen, and 2 mr at the sacrum. When treating the chest, back, and face for acne with a total dose of 425 r, a similar reduction in the "gonad dose" was obtained by the use of a cone. Lowering of the "gonad dose" was obtained with the use of a lead-rubber shield to the abdomen. (Fig. 6).

When we treated skin eruptions of the hands and feet in the range of 50 to 100 r doses and with the patient seated at the table, the dosimeters registered 10 mr at the groin, 100 mr on the abdomen, and 3 mr at the sacral area (Tables 2 and 3). With the use of 8 in. diameter copper cone the dose was significantly reduced, and with the additional use of lead rubber under the hands and in the lap, the dosimeters registered no radiation (Fig. 6).

In the treatment of the groin and perineum the testicular exposures were significantly high, even with conventional lead shielding. The dosimeters recorded as high as 1,420 mr for 150 r of treatment

TABLE 2.—*Quantity of Radiation Reaching the Groin, Abdomen, and Sacral Regions in Routine X-Ray Treatment of the Skin* *

Total Dose Treatment, r (mr)	Skin Areas Irradiated	Distance from Tube to Pubis, In.	Cone Used	Lead Shield	Average Recorded Dose, mr		
					Groin	Abdomen	Sacrum
100 (100,000)	Hands, back, & front	20	None	No	10.0	100.0	3.0
50 (50,000)	Hands, back	21	Copper 8 in. diameter	Lead rubber wrists	0.0	5	0.0
50 (50,000)	Hands, back	22	Copper 8 in. diameter	Lead rubber under hands	0.9	6	0.0
50 (50,000)	Hands, back	20	Copper 8 in. diameter	Lead rubber lap	0.0	1.0	0.0

* Factors used: Machlett tube—HVL 0.75 Al., 85 kv., 5 ma., 8 in. TSD (18.4 cm.);
Universal tube—HVL 0.35 Al., 80 kv., 5 ma., 10 in. TSD (24.4 cm.);
Landsverk dosimeters—range of 0-0.2 r., 0-2.0 r;
Victoreen minometer chamber—range of 0-10 mr.

TABLE 3.—*Quantity of Radiation Reaching the Groin, Abdomen, and Sacral Regions in Routine X-Ray Treatment of the Skin* *

Total Dose Treatment, r (mr)	Skin Areas Irradiated	Distance from Tube to Pubis, In.	Cone Used	Lead Shield	Average Recorded Dose, mr		
					Groin	Abdomen	Sacrum
50 (50,000)	Right ankle	38	None	Conventional	5.0	0.0	0.0
50 (50,000)	Left ankle	36	Copper 8 in. diameter	Conventional	0.0	0.0	0.0
150 (150,000)	Thigh & buttocks	8	None	Conventional	1420		
50 (50,000)	Buttocks	8	Copper 8 in. diameter	Conventional	80		
100 (100,000)	Perianal & perineal	6	Brass 1.5 in.	Lead foil, scrotum	138		

* Factors used: Machlett tube—HVL 0.75 Al., 85 kv., 5 ma., 8 in. TSD (18.4 cm.);
Universal tube—HVL 0.35 Al., 80 kv., 5 ma., 10 in. TSD (24.4 cm.);
Landsverk dosimeters—range of 0-0.2 r., 0-2.0 r;
Victoreen minometer chamber—range of 0-10 mr.

and 80 mr for 50 r of treatment. Even careful shielding of the scrotum with lead foil as described by Magnusson [27] did not reduce the dosimeter reading below 138 mr to the testicles. Therefore, these experiments were abandoned (Fig. 5 and Table 3).

In the three patients treated with small-cone applications for epithelioma or warts, and in which complete shielding could be accomplished, no readings were obtained in the dosimeters when using a skin dose of 1,500 to 2,000 r.

These measurements of x-rays and the reports of others are not meant to impart an appearance of mathematical exactitude, since the many unknowns and the areas of error are large. But they can give us a feeling of comfort and relief within the present air of fear and frustration.

If one takes the average of the higher readings in milliroentgens as recorded with the dosimeters in or around the gonadal areas (not directly at the ovary or testicle), it results in 33.0 mr (0.033 r) at any one treatment of 425 r for acne. Assuming 12 of such treatments may be had at weekly intervals, a total dose of 0.396 r might occur. This figure can be reduced by the use of a copper cone to 0.245 r exposure and still further be reduced by the use of an abdominal lead shield (Table 4).

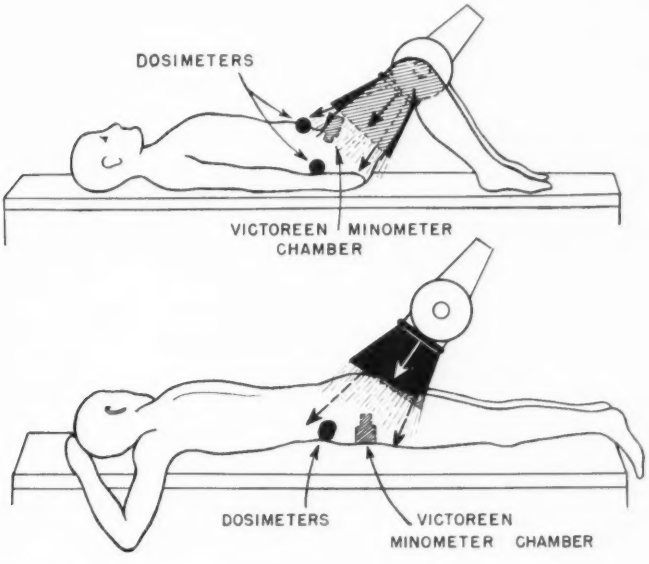


Fig. 3.—Method of measurement of radiation.

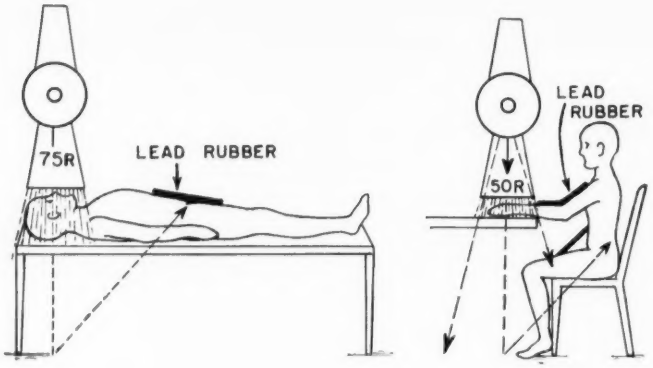


Fig. 4.—Methods of protection using a cone and lead rubber.

In the use of x-radiation to the hands in the sitting position the gonadal area may receive an average dose of 0.038 r at any one treatment of 100 r or for a total of six such treatments, 0.228 r. This figure can be reduced by proper shielding with lead and the use of a copper cone to 0.138 r (Table 4).

Neither the higher (0.396 r) nor the lower figure (0.138 r) even approaches the presumed reasonable estimate of 10 r as the reproductive life time dose of man-made radiation, which has been recommended as the maximum permissible dose by the National Academy of Sciences.[1] If multiplied 10 times it still falls far short of the 50 r, which is the top dose that should be considered for the *individual person*. If the total gonadal dose were to be used up entirely by the dermatologic therapy described here, it would require 25 courses of x-ray treatment for acne and 43 courses of treatment for the hands, within the span of the first 30 years of life, to affect seriously the mutation rate in these persons.

While these estimates may give at the present time some comfort to us, one cannot deny, in view of the evidence at hand, that any dose of x-ray to the gonads may in the distant future produce harmful mutations.[6] Thus every effort must be made to minimize the human exposure to man-made radiation. As such it is both reasonable and proper for the dermatologists to use methods and means by which reduction in gonadal dose can be had.

In this light and reading from our findings we would suggest that the following techniques be employed, in order to reduce this hazard:

1. Reduction of the gonadal dose when treating the patient in the prone position can be had by (*a*) the use of a metal (copper, lead, or iron) cone in all treatments, (*b*) lead shielding of scalp and chest, (*c*) lead shielding of the lower abdomen and groin, (*d*) sheet lead under the treatment table or the use of a metal (iron) table top.

2. Reduction of the gonadal dose when treating patient in the sitting position, can be had by: (Fig. 6). (*a*) the use of a metal (copper, lead,

TABLE 4.—*Quantity of Radiation Reaching the Groin, Abdomen, and Sacral Regions in Routine X-Ray Treatment of the Skin* *

X-Ray Dose, r	Total Estimated Gonad Dose, mr	Treatments, No.	Total Estimated Dose for Course of Treatment, r
	No Cone		
425 to face	33.0	12	0.396
100 to hands	38.0	6	0.228
	With an 8 In. Diameter Copper Cone		
425 to face	20.4	12	0.244
100 to hands	23.0	6	0.138

* Factors used: Machlett tube—HVL 0.75 Al., 85 kv., 5 ma., 8 in. TSD (18.4 cm.);
Universal tube—HVL 0.35 Al., 80 kv., 5 ma., 10 in. TSD (24.4 cm.);
Landsverk dosimeters—range of 0-0.2 r., 0-2.0 r;
Victoreen minometer chamber—range of 0-10 mr.

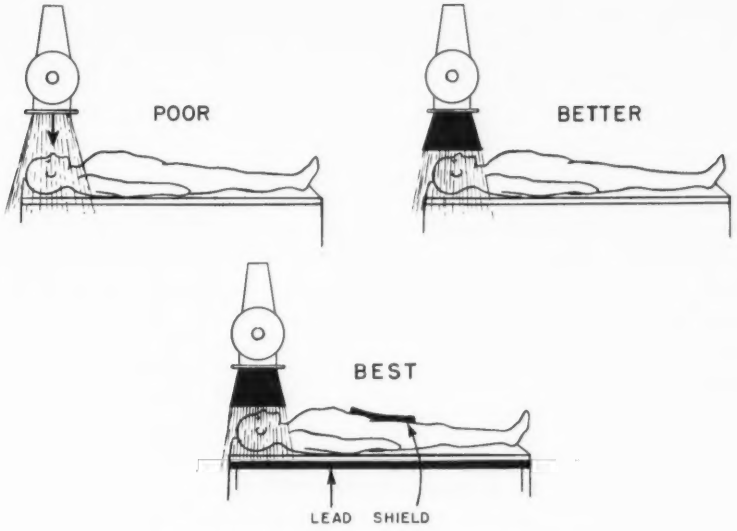


Fig. 5.—Methods of protection in x-ray treatment.

iron, or brass) cone in all treatments, (*b*) lead shielding of arms and lead shielding in the lap, (*c*) sheet lead under the table or the use of metal (iron) table top (in all instances the reduction of the total dose as much as possible consistent with good therapeutic principle).

3. The abandonment of x-ray therapy to the groin or perineum in patients under 30 years of age, unless shielded by a small cone (Fig. 3).

Summary

It has been our intention herein to point out that at the present there is more fear than fact in the recent statements, both in the medical and in the lay press, that the proper use of therapeutic x-rays have endangered or will endanger the progeny of

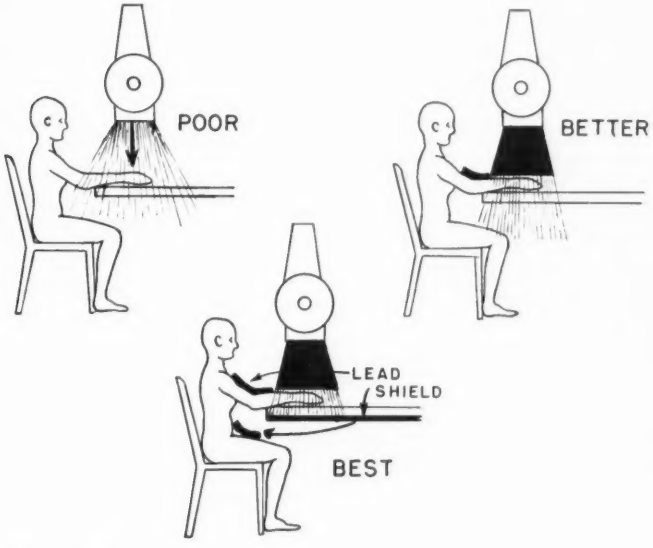


Fig. 6.—Methods of protection in x-ray treatment.

the human race. However, this is but a small part of the whole complex picture of radiation exposure, which has been only cursorily reviewed here.

It is very evident from our experiments as well as others that some x-radiation does reach the gonads in the use of therapeutic x-ray to the skin. But by direct measurement this quantity of x-rays to the individual patient is well below or within the reasonable limits of that advised by governmental authorities for the maximal permissible dose for those in atomic industry or for the public at large.

It seems apparent, from these observations, that there are at hand some measures which we should use that will materially reduce the quantity of x-rays reaching the gonadal area. Such measures are (1) the use of cones in all treatments; (2) the consistent and better use of lead shielding to the lower body, particularly the lower abdomen; (3) the use of lead on, or under, the treatment table; (4) the abandonment of antiquated x-ray machines.

The manufacturers of x-ray equipment also bear some of the responsibility for protection of the patient by improvement in the metal housing of the x-ray tubes and the use of lead, or iron, under, or on top of, the treatment tables. Lastly, the dermatologist should recognize such new developments in equipment and use it and be sure that the machines and his treatment measures are accurately calibrated.

Just as we are cognizant that any radiation to the gonads has been shown by inference to produce harmful mutations, we also recognize that such a constantly changing body of knowledge as represented in the practice of medicine should require us from time to time, as such questions arise, to readjust and reassess our therapeutic methods. Thus, we do not feel any guilt for the past use of therapeutic x-ray nor do we fear for its future value. Neither do we consider it necessary or wise to abandon atomic energy in the practice of medicine.

Finally, since attention has been repeatedly drawn to the fact that the genetic effects of x-ray are cumulative and delayed even in small doses, equally so are the genetic effects of our sexual and social habits and trends.[28] Recent attention to the effects of tight clothing by Americans and Europeans on the mutation rate indicate that the genetical hazards of wearing trousers may be a 100 to 1,000 times greater than those estimated from different sources of radiation.[29] It is possible we may have to resort to codpieces and kilts to save our progeny from harmful mutations. But be of good cheer. Man will undoubtedly not embrace either eugenics or genetics but will more likely embrace the first pretty woman he meets.

1293 Peachtree St., N. E. (3).

REFERENCES

1. The Biological Effects of Atomic Radiation: Summary Reports, National Academy of Sciences, National Research Council, 1956.

2. The Hazards to Man of Nuclear and Allied Radiations: Report to the Medical Research Council of Great Britain, London, Her Majesty's Stationery Office, June, 1956.

3. Muller, H. J.: Radiation Damage to Genetic Material, Am. Scientist 38:33 (Jan.) 1950.

4. Muller, H. J.: Damage to Posterity Caused by Irradiation of the Gonads, Am. J. Obst. & Gynec. 67:467 (March) 1954.

5. Muller, H. J.: Genetic Damage Produced by Radiation, Science 121:837 (June 17) 1955.

6. Crow, J. F.: Possible Consequences of an Increased Mutation Rate, Eugenics Quart. 4:67 (June) 1957.

7. Schubert, J., and Lapp, R. E.: Radiation: What It Is and How It Affects You, New York, The Viking Press, 1957.

8. Pauling, L.: Petition Urging the Agreement to Stop Nuclear Tests, Science 127:277 (Feb. 7) 1958.

9. Rall, J. E.: Radiation and the Medical Profession, Editorials, A. M. A. Arch. Int. Med. 100:347 (Sept.) 1957.

10. Maximum Permissible Radiation Exposures to Man: A Preliminary Statement of the National Committee on Radiation Protection and Measurement, A. M. A. Arch. Int. Med. 100:353 (Sept.) 1957.

11. Statement by The United Nations Scientific Committee on the Effects of Atomic Radiation:

The Responsibilities of the Medical Profession in the Use of X-Rays and Other Ionizing Radiation, J. Nat. Cancer Inst. 18:481 (March) 1957.

12. Beamer, P. R.: The Responsibilities of the Medical Profession in the Use of X-Rays and Other Ionizing Radiation, Am. J. Clin. Path. 27: 567 (May) 1957.

13. Statement by the United Nations Scientific Committee on the Effects of Atomic Radiation: The Responsibilities of the Medical Profession in the Use of X-Rays and Other Ionizing Radiation, J. Pediat. 50:372 (March) 1957.

14. Taylor, L. S.: The Philosophy Underlying Radiation Protection, Am. J. Roentgenol. 77:914 (May) 1957.

15. Neel, James V.: The Delayed Effects of Ionizing Radiation, J. A. M. A. 166:908 (Feb. 22) 1958.

16. Crossland, P. M.: Dermatological Radiation Therapy in This Nuclear Age—An Appraisal, J. A. M. A. 165:647 (Oct. 12) 1957.

17. Laughlin, J. S.; Meurk, M. L.; Pullman, I., and Sherman, R. S.: Bone, Skin and Gonadal Doses in Routine Diagnostic Procedures, Am. J. Roentgenol. 128:961 (Dec.) 1957.

18. Chamberlin, W. E., cited in Importance of Chest X-Rays in Total Radiation Exposure, Tuberc. Abstr. 30:1 (Jan.) 1957.

19. Witten, V. H.; Sulzberger, M. B., and Stewart, W. D.: Studies on the Quantity of Radiation Reaching the Gonadal Areas During Dermatologic X-Ray Therapy: I. Preliminary Report, J. Invest. Dermat. 28:187, 1957.

20. Witten, V. H.; Sulzberger, M. B., and Stewart, W. D.: Studies on the Quantity of Radiation Reaching the Gonadal Areas During Dermatologic X-Ray Therapy: II. Methods, Quantitative Measurements, and Analyses of Some Important Factors Influencing the Gonad-Dose, A. M. A. Arch. Dermat 76:683 (Dec.) 1957.

21. Stewart, W. D.; Witten, V. H., and Sulzberger, M. B.: III. Shielding Techniques and Other Precautions for Reducing the Gonad Dose, presented at 18th Annual Meeting of the Society for Investigative Dermatology, June 1-2, 1957, New York, to be published.

22. Welton, D. G.: X-Ray Therapy in the Private Practice of Dermatology, South. M. J. 50:648 (May) 1957.

23. Callaway, J. L.; Moseley, V., and Barefoot, S. W.: Effects of Roentgen Ray Irradiation on the Testes of Rabbits: Possible Harmful Effects on Human Testes from Low Voltage Roentgen Ray Therapy, Arch. Dermat. & Syph. 56:471, 1947.

24. Purser, P. R., and Qurist, C. F.: An Estimate of the Genetic Dose from Radio-Therapy, Acta radiol. 48:267 (Oct.) 1957.

25. Hine, G. J., and McCall, R. C.: Gamma Ray Backscatter, Nucleonics 12:27 (April) 1954.

26. Flaty, J., and Maudal, S: Some Measurements of Scattered Radiation from Diagnostic Beam, Acta radiol. 46:680 (Nov.) 1956.

27. Magnusson, W.: A Device for the Protection of the Testicle in Roengten Examinations of Adjacent Organs and Bones, Acta. radiol. 37:288, 1952.

28. Teller, E., and Latter, A. L.: Our Nuclear Future, New York, Criterion Books, 1958.

29. Ehrenberg, L.; Ehremstein, G., and Hedgren, A.: Gonad Temperature and Spontaneous Mutation Rate in Man, Nature, London 180:1433 (Dec. 21) 1957.

ABSTRACT OF DISCUSSION

DR. MARION B. SULZBERGER, New York: I have not prepared any written discussion, because, while I had the previlege of reading these papers (the one by Dr. Andrews and Dr. Domonkos just yesterday and Dr. Alden's paper some time before), I did not know until just now what Dr. Cipollaro and the other discussers would say and I did not want to bore you by needless repetition. Therefore, while sitting and listening, I just jotted down a few notes on several additional points that I thought might be worth discussing.

I think that these findings are essentially the same as mensurations that were yielded by Callaway's early studies with the cruder methods then available and by those of Witten, Stewart, and me more recently. I hope that I can say that our studies, too, led to inferences which had the same quantum of common sense as that which you have heard now from the presenter.

There are lots of ridiculous fears and exaggerated ideas in this field on the part of every segment of the public, including the medical public. For example, I have encountered among my patients old ladies of 60 and even 70 years plus, who come in and say they will not allow any x-ray to any part of their anatomy because they are worried about their grandchildren and the future of the race. Many of these fears are just about as sensible as would be my fear of putting on my trousers in the morning because it might elevate the temperature of certain parts.

We know that through years of careful studies and of experience (and sometimes unfortunate experience) we have not only a shrewd idea but a pretty accurate estimate of the dosage limits which should be adhered to in giving radiation to each kind of skin disease and each skin site (Sulzberger, M. B.; Baer, R., and Borota, A.: Do Roentgen-Ray Treatments as Given by Skin Specialists Produce Cancers or Other Sequelae? *A. M. A. Arch. Dermat. & Syph.* 65:639 [June] 1952). With the modalities that we use, with the modern mensuration and safety factors that we

use, we know what is safe dosage insofar as local damage to other underlying structures (such as the bones and bone marrow) is concerned. But we do not know what the optimal dose is to the gonads in man.

I hope that you will note that I said "optimal dose." I used these words because we must realize that the human race advances, undergoes the advances of evolution, through mutation. Some purists and cynics may hold that I am not justified in saying "advances." I should, perhaps, say "changes" or "undergoes modulations," to use Dr. Montagna's and Dr. Pinkus' more modern term. But that change of words does not change the fact that without cosmic rays and rays from radioactive elements in the earth and other sources of radiation to man's testes (because the rays to the testes probably play the greatest role, these organs being much more exposed than the ovaries) we might all still be pelting each other with coconuts or dragging our spouses around by their hair through the primeval forests.

The question is, how much acceleration of mutation is beneficial? Muller and others estimate that 1,000 harmful mutations occur to every single beneficial one. That is because mutations are all in a sense random *errors* and, by laws of chance, there may be a beneficial one in only a small fraction of instances.

In primitive society, this situation was not as bad as now. The accumulation of harmful genes did not occur so rapidly, because the harmful mutants were lethal or partially lethal and died out in the main before they could reproduce. In our society, with medical knowledge and with all the new devices for preserving life and enabling handicapped persons to survive to the age of reproduction (for instance, those with diabetes), not only is the mutation rate being increased by man-made radiation, but we are also preserving and increasing the pool of harmful mutants in our society. But we do not know how much, if any, acceleration still would be beneficial.

In the face of this ignorance and the probability of harmful mutations accumulating at too rapid a rate, it behooves everyone in medicine to reduce the gonadal dose of man-made radiation to the utmost possible minimum. Those are the reasons for the studies of Callaway, Witten, Stewart, and me; of Cipollaro, Kallos, and Ruppe; of Andrews and Domonkos, and now of Herbert Alden.

I think, also, it goes without saying that *no one* should give any *unnecessary* x-ray treatment and one should always use all the modern shielding devices and protective devices that we now know (*and* that undoubtedly will be discovered in the next few years because I am sure that many further studies will be forthcoming in this area).

In general, I would say that softer rays are safer than harder ones, and that for this reason the grenz ray surely has a greater future. The same applies to some degree to thorium X. Moreover, for most superficial therapy, x-ray machines operating at 20 to 40 kv. will probably prove most safe and effective.

DR. CHARLES C. DENNIE, Kansas City, Mo.: From 1786 to 1801, there was a physicist at Ballston Pool, N. Y., by the name of T. Gale, who was the first one in America to utilize electricity in the treatment of disease. He called it "electric shock treatment for the insane." At that time, there were some static machines made in England and in the Netherlands which did not work, and Gale himself built his machine out of a glass cylinder, in a wooden frame, which was turned by hand. Beneath this cylinder, there was a piece of satin. Below it was a deerskin, impregnated with lead and pewter, and from that led three fingers of iron wire that practically touched the cylinder. The current was then carried to a Leyden jar, with two outlets to this thing.

He was the first one to measure the spark gap. He produced a spark gap of 4 in. in this Leyden jar. He put a connecting chain on the shoulder or the head of the patient and placed the other pointed terminal next to the skin. He made an electronometer of corks, and, as the current was increased in the machine, these little pieces of cork, which were fastened to 8 in. linen threads, spread out until they were entirely in one plane. That was as much current as he could produce, but that current was too heavy for any patient, so he reduced the current down to the maximum dose for any person. His principal treatment was of the insane, by the shock method.

He also devised the diathermy table, a crude sort of affair in which he introduced heat into his patients. He sharpened one of the terminals and charred malignancies on the face and on the breast, and, as he said, his first patient was himself, as he had a rose cancer on his face.

He was the first great physicist in this country, although we give the credit to Benjamin Franklin. Benjamin Franklin was his friend and consulted with him in the manufacture of this static machine, but T. Gale was the great physicist of this country and was the equal of Priestley and Lavoisier, who came along about the same time. He not only manufactured this machine, but he also studied gravity, the tides, the magnetic currents, and all that sort of thing and spent a good part of his book in the investigation of these things.

I picked up this book by chance and had to confirm that this man was real. The first place I approached was the Library of Congress. I asked them if such a book were there and if so, to

give me a photostatic copy of it, which they did. Then, I sent Mrs. Dennie to Ballston Pool, which is the name of the place in which Gale resided. She had an experience almost like that of the "Old Man and the Sea" in tracing down the origin of this book. I will not go into the details, but it took her three days to finish her investigation and to locate a single copy in the Academy of Medicine of New York. There is one copy besides that. There are four copies in the world today. But T. Gale was the originator of the machines by which later x-ray was produced.

As to the beginning of x-ray therapy in the United States, there has been some question. I am at the present time writing the biographies of three men in my town whom I call the cow-town doctors. The interest lies in many directions, but in this research work I investigated the hospital records of St. Joseph Hospital, and, much to my surprise, the sisters gave me a reprint of their published book for the year 1900 and 1901, in which there was an article concerning x-ray therapy. There is a clear photograph of Dr. Scott and two of his nurses treating a cancer of the breast, in 1900, with irradiation. There is this small tube above the table, and there is Dr. Scott with his two nurses, all of them well within the limits of dangerous doses of irradiation. Dr. Scott had both his hands amputated within a few years and lost his life a few years later. Whatever happened to these other people who were exposed to irradiation, I don't know.

There were at least two years of experiments with this x-ray before they wrote the article, and they came to the conclusion that the treatment of cancer was best accomplished by a combination of x-ray and surgery. I am sure that they started that treatment at least in 1898.

As to the appearance of x-ray in this country, there were two tubes shipped to Boston. When I was a youngster, in 1897 or 1898, I don't know which, there was a traveling showman who came through our village. He had an x-ray machine run by batteries. He had one of the old-time fluoroscopes, and I well remember the first one who came up to have his hand examined. He was a Negro. I looked in the fluoroscope and saw a bullet in his hand, which was acquired in the Civil War, as he was one of his colonel's attendants. There was also an old negro woman who came in and looked in the fluoroscope. She was very fat; she hustled away rapidly because, as she said, "This is no place for a decent colored woman in nothing but a calico dress."

I related this experience in Florida three years ago, and two things happened. A well-known neurologist by the name of Woods told me that that man whom I had seen with the x-ray machine back in 1898, he was sure, was then still living. He was a patient of his. We three had luncheon together. When I saw the old man, it wasn't the same one, but he knew the other fellow. They both started out at the same time with an x-ray tube, which was called a Queen's tube, touring the country and charging for the show that they put on. He ran the machine with wet batteries. He knew a good deal about the physics of x-ray. He knew that a slight amount of atmosphere that remained in the tube must be ionized. The current would often run over the top of the tube, and he would break the current by putting his right forfinger on the tube. That finger was withered down to the bone. He had a 100 x-ray keratoses on his face.

He told me that he had tried to interest the doctors in the x-ray machine but could not do it. When the cinema came in, he quit the x-ray in order to devote his entire time to show business.

Clinical Evaluation of Antipruritic Drugs

Consideration of Orally or Parenterally Administered Agents

FRANK E. CORMIA, M.D., and JOHN W. DOUGHERTY, M.D., New York

Recently, an attempt was made to evaluate the antipruritic effect of an analgesic drug. Some of the problems encountered will be discussed, and a blueprint for the proper clinical investigation of antipruritic drugs will be presented.

Experimental Procedure

In previous animal experiments, the drug was found to depress the perception of cutaneous stimuli. In addition, it was found to have potent local anesthetic activity, mild antihistaminic action, and potentiation of analgesia.

The case material consisted of patients with severe chronic pruritus. In a pilot study on 23 patients, the drug showed considerable promise, and a subsequently administered placebo was ineffective. The experiment was then continued with 79 additional cases, with use of a carefully planned, double-blind, randomized technique. Statistical analysis of the complete data demonstrated that the test drug was not superior to the placebo. Appreciation of the difficulties and pitfalls inherent in the study led to a critical examination of the entire experimental procedure. A study was then made of 25 reports published in the past 15 years on the effects of orally or parenterally administered antipruritic agents.

Definition of the Problem

Theoretically, the utilization of a drug for the control of itching should be a simple procedure:

Drug Plus Subject=Response.

A drug which has shown good therapeutic and low toxic effects in base-line animal experimentation is chosen for trial in man. Preliminary experiments are conducted, preferably by several independent investigators, to determine optimum dosage for maximum therapeutic effect commensurate with safety. Large-scale clinical trials are then made; if the results seem promising, the drug is marketed and promoted to the medical profession.

Most of the agents recommended for the control of itching during the past two decades have not stood the test of time. Many have been discarded, and the continued use of several of the remaining ones has been dictated not so much by the results obtained as by the desire to prescribe something for the complaining patient. It is true that pharmaceutical houses tend to promote their products in glowing terms, but this is due more to absence of liaison between advertising and scientific divisions of the company than to actual misrepresentation. The chief blame for the promotion of inferior antipruritic agents must be laid at the door of the medical teams making the preliminary investigations. No physician would deliberately falsify his experimental studies; it follows that exaggerated claims for a drug are the result of inadequate investigative techniques.

The problem was first brought to the attention of the dermatological profession in 1950, by Pillsbury, Zimmerman, and Baldridge [1] in a masterful report, although previous warnings had been given in statistical treatises.[2] Livingood again touched upon the subject in a more general discussion of clinical investigation in dermatology.[3] Albritton summarized his earlier

Submitted for publication July 16, 1958.

From the Department of Medicine (Dermatology), New York Hospital-Cornell Medical Center.

This work was supported in part by a grant from Merck Sharpe & Dohme, Division of Merck & Co., Inc., Philadelphia.

Read before the 78th Annual Meeting of the American Dermatological Association, Inc., Sun Valley, Idaho, June 6, 1958.

observations in a recent report on "The Six Unities of Medical Research." [2] More recently, Bross,[4-6] Moyer,[7] Beecher,[8] and others have examined the individual phases of the problem and made suggestions for their control.

Pillsbury and his associates pointed out that clinical experiments are difficult to control and the measurement of results is often unreliable. They emphasized that faulty design in an experiment may make accurate conclusions impossible, and that the result obtained may be due to an associated agent or to chance rather than the agent studied. Under associated agents they listed time (normal course of disease), heat, light, hospitalization, systemic status, enthusiasm of investigator, bias, and pressure from grantors. They stressed the difficulties of subjective measurements, especially of itching, and the lack of a control standard by which to measure results. Finally, the Pillsbury group analyzed seven different categories of disease or specific therapeutic modalities and concluded that evidence of therapeutic effectiveness could not be substantiated in the protocols of others or in their own experiments.

Critical Analysis of Problem

The various factors which may influence the accuracy of studies on antipruritic drugs may be considered under several headings, as follows:

1. Selection of case material.
2. Control of associated factors.
3. Placebo control.
4. Administration of drug and placebo.
5. Interpretation of treatment response.
6. Reproducibility of results.
7. Elimination of chance variations.

1. *Selection of Case Material.*—A careful selection of cases is essential in experiments dealing with the effect of a drug on itching. One must select patients who are likely to finish the experiment, who will carry out therapy as instructed, and who have sufficient discernment to estimate treatment response subjectively. Patients who tend to react to any type of medicine can be identified by the placebo control, but they are generally undesirable as test subjects. In serious, rapidly progressive, or potentially incapacitating diseases, the decision as to whether the drug may be given in fairness to the patient must be made.

With regard to suitability of disease, it is essential that the patient have a *chronic* moderate to severe pruritus. Those with diseases having an erratic or self-limited course, such as urticaria or pityriasis rosea, should be rejected. It is best to eliminate cases with contact dermatitis. A "placebo" ointment may cure such cases, and failure to eliminate the contactant may negate drug effects. Diseases in which specific therapy must be given concomitantly, such as severe dermatitis herpetiformis, pemphigus, or pyoderma where infectiousness is a factor, also should be eliminated. The criteria of suitability should be determined objectively; physician bias at this point can wreck an otherwise well-constructed experiment. Adherence to these criteria, while essential for accurate determination of drug effect, is difficult in actual selection of material. One hundred patients with severe itching may be obtained from an average clinic in a relatively short period; however, in fulfilling the above requirements, nearly a year was required to accumulate the 102 patients in the present series.

2. *Control of Associated Factors.*—The control of all associated agents which may influence the course of the disease and the severity of itching is impossible. A patient with an itching dermatosis demands and expects a local medication; in the present series a bland inert ointment with a slightly acid pH was prescribed. Undoubtedly, this helped some disorders and aggravated others. These effects may be expected to cancel each other out in long-standing pruritic diseases. Patients who require hospitalization should be rejected unless the entire series has been hospitalized and has not benefited from previous therapy. The series should be conducted so that the effects of cold, heat, humidity, and seasonal

changes are kept to a minimum. For example, sweat retention in hot humid weather may aggravate the itching of erythroderma and a false-negative drug effect may be obtained. A spring-to-summer experiment likewise suffers in that exposure to warm sunlight and the psychological uplift of pleasant weather may impart to the drug an unwarranted curative property. Subjective factors, such as psychological state, insomnia, and the presence of severe systemic disease (hepatitis, nephritis, lymphoma, etc.), may introduce further variables into the experiment. Yet it would be unwise to reject patients with such conditions, since they are prime candidates for antipruritic drugs. The most important of the associated agents is the influence of suggestion. While this cannot be eliminated, many of its aspects can be controlled. Detached impersonal handling by laboratory personnel and the responsible physicians is essential. An oversympathetic desk clerk or technician can influence experimental results. The attitude of the physician is even more important. Enthusiasm for the new product must be avoided, and no attempt to establish rapport or lend a sympathetic shoulder should be made. Finally, laboratory studies in the experiment should be kept to the necessary minimum. A patient gains a false idea of the potency of a drug if an elaborate battery of laboratory tests is conducted at each visit.

3. *Placebo Control.*—Many of the difficulties in clinical testing can be eliminated by the use of placebos and a double-blind randomized technique. The indications for placebos in drug testing have been recently summarized by Moyer.[7] Placebos may be life-threatening when one is dealing with drugs having a profound pharmacologic effect. For example, when dealing with hypotensive agents, it is important that the physician know when the active drug is being given. The drug should not be employed in a blind experiment in preliminary trials. Dosage requirements must be established and toxic and allergic effects evaluated. If strict individualism of dosage is required, blind studies should not be used. A double-blind study should not be made if the drug has potentially damaging effects. When placebos are not disadvantageous to the patient, and when the effect of the drug is mainly on the nervous system, their use is generally considered essential.[4-7] Placebos are necessary to rule out the effects of suggestion and have been deemed important in patients with neurotic tendencies or psychogenic pruritus. However, analysis of our material showed that the effects of suggestion operated uniformly, regardless of whether the patient had a psychogenic, nonpsychogenic, or mixed type of pruritus. In a blind study, the patient does not know which tablet is drug and which is placebo, whereas in the double-blind study, neither the patient nor the physician knows which medication is given. In studies on itching, when the drug has only moderate potency, double-blind studies are essential. This technique serves as an effective check on inexperienced personnel, investigator bias or overenthusiasm, and grantor pressure. The use of subjective criteria for the evaluation of improvement can be controlled only by the double-blind method.

4. *Administration of Drug and Placebo.*

Drug and placebo should never be given in a regular sequence. An especially pernicious practice is first administration of drug, followed by the placebo. Administration of drug and placebo should be randomized. In a randomized series of 100 patients, the drug or placebo will be given first in about 50 instances; this sequence, being left to chance, is not a regular one. A regular sequence introduces several adventitious factors in the procedure or personnel setup. Randomization minimizes also a possible effect of the drug, when given first, on the effect of the placebo. Moreover, it balances the initial suggestive effect of the drug or placebo. In our preliminary series, when the drug was given first, 13 of 23 patients were improved, while only 3 of 17 patients subsequently given the placebo

TABLE 1.—*Influence of Time of Medication on Results Obtained*

Sequence of Therapy	Improved	Not Improved or Worse
Drug first	26	6
Placebo first	20	10
Drug second	10	19
Placebo second	12	26

were benefited. In our double-blind series, the importance of first administration is shown in Table 1.

5. *The Interpretation of Treatment Response.*—Evaluation of improvement in studies on itching is not easy. The main difficulty is the absence of an objective standard of comparison. There is no drug now available which exerts a constant effect on itching. In a previous study, the use of itch threshold determinations with histamine was suggested as a tool for the measurement of itch. However, the itch threshold is not dependably constant. It may vary with changes in time of day, temperature, and emotional status.[9] Furthermore, the results of a two-hour test cannot be equated directly with those following the therapeutic administration of a test drug over a longer period. Such a comparison was attempted but had to be abandoned.

Since the treatment response must be estimated subjectively by the patient, a standard scale of reference is essential. In previous studies, responses have been listed according to the result (poor, fair, good, or excellent), or to the degree of improvement (none, mild, moderate, excellent, and cure). In our material, results were tabulated originally according to the degree of improvement. With this scheme, difficulty was experienced in comparing the results obtained with Treatment 1 and Treatment 2. For example, during the second week of treatment, the patient might have more itching than during the first week but still have improvement over the original observation. Thus, the patient could be either improved or worse, depending on the point of reference. Equal difficulty was encountered in patients who showed moderate improvement in the first week and no change in the second. Does this evidence indicate that the antipruritic effect of the second medication maintained the initial improvement, or that no effect on itching had occurred? As has been pointed out elsewhere,[10] itching may be perpetuated in an interrelated cycle when the precipitating cause has been removed. If the cycle is interrupted by anti-inflammatory agents, antipruritic drugs, suggestion, or by adventitious factors, it may or may not recur. Thus, the course of itching over a period of time may show remarkable variations.

For our double-blind studies, a scale of treatment responses based on the degree of itching was devised. Patients were asked how much itching they experienced during a given test period, without reference to previous severity. Itching was graded as none, mild, moderate, or severe. The use of gradations such as very mild or very severe were found to be impractical. Patients were checked at weekly intervals. The results were then compared to those obtained in a daily check sheet kept by the patient. There was good correlation between the daily and the weekly check sheet in some 65% of our material. In the remainder the daily check sheet seemed more accurate but was more difficult to interpret, since there was irregular variation in the intensity of the itching. A regular trend was unusual. In a few instances, a four-hour diary was employed. This diary, used in a two-day experiment, was of no value, entries often being omitted. It is probably suitable only in hospitalized groups, when the check is made by the physician or his trained representative.

Patient reliability is an important consideration in estimating treatment response. In our group, reliability was estimated in 83 patients; it was considered good in 67, fair in 15, and poor in 1. Despite all precautions, patient reliability cannot be entirely controlled. The physician's inter-

pretation of treatment response is all-important. If possible, the study should be made by a single investigator. Many inaccurate reports in the past have stemmed from doctor enthusiasm and bias. This may be due to pressures from the grantor or salary considerations. Often, continuation of a grant may depend on results obtained in a given period. Pharmaceutical firms are naturally hopeful of a favorable report on a drug in which funds have been invested, and the pressures which they unconsciously exert are incalculable. The investigator's attitudes may be reflected both in the method of presentation of the test drug to the patient and in the physician's estimate of treatment response.

6. *Reproducibility of Results.*—Theoretically, partial or complete suppression of itch by a drug should be reproducible. Frequently, repeated drug trials are not feasible, since they must be conducted after the conclusion of the initial double-blind study. When possible to obtain, a reproducible effect greatly increases the reliability of the preliminary findings.

7. *Elimination of Chance Variations.*—When all precautions have been taken to insure that the quality of the information obtained is sound, the material should be subjected to analysis by a statistician. As Bross has emphasized,[4-6] the statistical device can extract information but cannot add information. Misinformation in the basic data is extracted right along with correct information by the statistical method. With correct basic data, one may eliminate, ordinarily with a 5% level of error, the results due to chance variation. When our material, studied on the basis of frequency and degree of improvement, was subjected to analysis, the differences between drug and placebo did not reach the customary 5% level of significance.

Blueprint for Studies on Pruritus

The following blueprint for the investigation of the antipruritic effects of drugs is submitted:

1. Preliminary drug trials to determine optimum dose, toxicity, and sensitization potential.
2. Large-scale clinical trials (100 or more patients, unless dealing with an extremely potent drug).
3. Double-blind study.
4. Randomization.
5. Selection of patients on basis of general and disease suitability.
6. Control (and elimination, if possible) of associated factors, especially doctor bias.
7. Standard scale of subjective response.
8. Elimination of chance variations.
9. Reproducibility of results.
10. Preliminary evaluation of plan by expert statistician.

Analysis of Twenty-Five Reports Dealing with Drugs Given Orally or Parenterally for Pruritus

Twenty-five reports on the use of drugs for the control of pruritus have been analyzed. Some of these studies have been widely quoted and have undoubtedly influenced current dermatological therapy for pruritus. Each report has been evaluated by the criteria presented for a blueprint for further studies on pruritus. Deficiencies in the acquisition of basic data, and in the statistical analysis of this data, are shown in Table 2.

Summary

An analysis is made of the use of drugs given parenterally or by mouth for the con-

TABLE 2.—*Analysis of Twenty-Five Reports on Antipruritic Drugs (Orally or Parenterally Administered)*

Criteria Utilized in Study	Compliance with Criterion		
	Yes	Not Noted	No
Preliminary evaluation by statistician	—	2	23
Double-blind study	1	—	24
Randomization	—	1	24
Partial placebo control	2	1	22
Adequate no. subjects	8	—	17
General suitability of patient	4	12	9
Suitability of disease	9	1	15
Control of adjunctive therapy & associated variables	3	9	13
Reproducibility of improvement	2	—	23
Statistical elimination of chance variations	1	—	24

trol of itching. Difficulties encountered in a recent personal study are summarized. A blueprint for the control of future studies is submitted. Twenty-five reports dealing with antipruritic agents are analyzed and compared with criteria suggested for an ideal experiment.

1070 Park Ave. (28).

REFERENCES

1. Pillsbury, D.; Zimmerman, M., and Baldridge, G.: Experimental Controls in Clinical Dermatologic Investigation, J. Invest. Dermat. 14:359 (May) 1950.

2. Albritton, E. C.: The 6 Unities in Medical Research, J. A. M. A. 161:328 (May 26) 1956.

3. Livingood, C.: Clinical Investigation in Dermatology, J. Invest. Dermat. 25:203 (Oct.) 1955.

4. Bross, I.: Therapy for Intellectual Obesity or Common Sense in Reducing Figures, Am. J. Obst. & Gynec. 69:372 (Feb.) 1955.

5. Bross, I.: Statistics and the Clinician, Ann. Int. Med. 43:442 (Aug.) 1955.

6. Bross, I.: Memo-Outline of Format.

7. Moyer, J.: Psychosomatic Problem in Drug Evaluation, A. M. A. Arch. Int. Med. 98:608 (Nov.) 1956.

8. Beecher, H.: Appraisal of Drugs Intended to Alter Subjective Responses, Symptoms, J. A. M. A. 158:399 (June 4) 1955.

9. Cormia, F., and Kuykendall, V.: Experimental Histamine Pruritus: III. Influence of Drugs on the Itch Threshold, A. M. A. Arch. Dermat. & Syph. 69:206 (Feb.) 1954.

10. Cormia, F.; Dougherty, J. W., and Unrau, S.: Proteolytic Activity in Dermatoses: Preliminary Observations on Inflammation and Pruritus, J. Invest. Dermat. 28:425 (June) 1957.

ABSTRACT OF DISCUSSION

DR. WALTER B. SHELLEY, Philadelphia: We are all indebted to Dr. Cormia for spelling out the principles of experimental design for the clinical testing of antipruritic drugs. He has given us a carefully reasoned and precise methodology for the rigorous testing of new compounds. As you saw, this included the careful selection of test patients, the reduction of extraneous factors, the use of the double-blind control, and, finally, statistical interpretation. All of this submerges the effects of physician bias and patient suggestibility, two prejudicial elements which have long accounted for many a solitary report on the specific virtues of a given drug.

I can add little to Dr. Cormia's penetrating analysis, but I should like to stress a significant area of activity which must precede this precise and controlled evaluation of an antipruritic drug. I refer to the preliminary testing period.

First, the investigator must come upon his drug by way of serendipity, intuition, or logic. He then proceeds to become acquainted with it, applauding each little success and worrying over every failure. At this stage, a solitary success is significant. Later statistics could and would dismiss any such isolated finding, but now the investigator is nurturing his idea, and baleful probabilities must be kept away. What does this success in a single patient mean? If the investigator can discern the exact mode of action, he can then explain the failures. We are dealing in the problem of pruritus with a heterogeneous situation. We are not dealing, say, with the treatment of something that is homogeneous, like the treatment of warts, and so that the investigator in this preliminary period has to take special pains to find out the precise indications for a drug. Then, he can clearly formulate specific conditions for testing, which would otherwise lead him into a situation where the effects would be hidden.

That single success—why? Is the compound an antipruritic like atropine in that it eliminates sweating and, hence, the pruritus of miliaria? Could it be acting as an anti-inflammatory agent like the corticosteroids or antihistaminics? Is it affecting only the patient's attitude rather than his sensory experience? Phenobarbital and possibly trimeprazine (Temaril) act as such antipruritic tranquilizers. Or is it truly producing the ability to perceive pruritus? This area remains full of promise.

Those failures—why? Is the dosage too low? Too infrequent? Should another route of administration be employed? Here, all the ingenious individuality of the investigator comes into full play. Can he but know his drug well enough, he can specify the precise indications so perfectly that his compound will show up well on the rigid, depersonalized double-blind routine. But, if he fails to catch the mechanism, his drug will remain buried under failures it should never have had to shoulder.

Thus, it is our feeling that the preliminary scout testing of any compound must be done as carefully and thoughtfully as the controlled clinical assay just described so well by Dr. Cormia.

DR. FRANK C. COMBES, New York: I also enjoyed Dr. Cormia's presentation very much, particularly the humor that he interspersed from time to time. He certainly has shown us many of the hazards to which one is exposed when one attempts to do a statistical study of any drug.

There are many more hazards. He himself said that he gave only some of them. We are constantly encountering new hazards in a study of this type. One thing we do not always appreciate is that

when a medication is taken by mouth, there is no proof in many instances that it has ever left the bowel and that it has ever got into the blood stream. Even in the blood stream, it does not necessarily mean that it acts, in spite of all the television stories of how much more quickly one medication acts than another because it is in the blood stream.

This came to my attention several months ago, when we had a patient who had leukoplakia and I was giving her some popular vitamin by mouth, a synthetic-type vitamin. It happened that she had also had a colostomy, and she came to me after her visit and said, "Those little pills that you gave me, I swallowed them, and they all came out in my colostomy wound." That surprised me, because these were supposed to be just sugar-coated. I talked with her, and she consented to be a subject for experimentation.

It was very surprising to find that when we gave her various coated pills and delayed-action medication many of them went right through her intestinal tract and then out the colostomy wound, undissolved.

Therefore, it is apparently essential that the medication be capable of disintegration, and it must also be essential that there is functional integrity of the gastric juices and the gastrointestinal tract.

Dr. Donald H. Williams, Vancouver, B. C., Canada: I feel that this paper has been one of the fundamental presentations of this meeting. Dr. Cormia has provided us with a criterial yardstick for measuring the soundness of certain types of clinical investigation and the validity of their conclusions. Undoubtedly, he has views as yet unexpressed about how these criteria should be applied.

I should like to suggest one application. As leaders who influence dermatological research throughout this continent, I believe we should strongly support and widely publicize Dr. Cormia's basic criteria with particular respect to the present widespread use of the public as the "guinea pig" for clinical trial of new products in a haphazard, uncontrolled, and costly (to the public) manner.

If the drug trade adhered strictly to Dr. Cormia's criteria in launching new products on the market, we would, to the benefit of all, see the end of the financial catharsis ladled out by the drug trade which propels half-baked research onward in a peristaltic rush of half-digested investigative roughage, most of which, fortunately, after precipitate publication, is quickly flushed into oblivion.

Dr. Rudolf L. Baer, New York: I enjoyed Dr. Cormia's presentation very much. I should like to ask him a question about the careful selection of the patients which he suggests. Does one not exert a strong bias by the very fact that one attempts to select the patients "carefully" for such a study, rather than taking any patient who complains of itching? Such a selection may be particularly risky, since one sets out to assay the patient's response to a drug which is designed to counteract a subjectively, rather than an objectively, observable manifestation of a dermatosis. It seems to me such careful selection might exert just the sort of bias that one is trying to avoid.

Dr. Frank E. Cormia, New York: Dr. Shelley has brought out the fact that these collateral factors in the use of antipruritic agents are extremely important. He also brought up the question of dosage. This is important. In our preliminary study, for example, we found that in the doses recommended, based on animal experiments, the drug had no effect whatsoever. However, when adequate doses were given, there was a high incidence of allergic problems. The dose must be carefully evaluated in the preliminary experiments.

Dr. Combes mentioned the matter of the drug reaching the site of itching. Ordinarily, when we receive a drug for testing, prolonged and reasonably thorough animal experimentation has been done and this point has been settled. Of course, as has been pointed out on many occasions, there are marked differences between the reactions of animals and humans. Not only that, but, with particular reference to itching, it is a pretty difficult thing, except to watch the animal scratch, to know whether it is actually itching and whether it has relief from itching when one gives a drug.

Dr. Williams brought out an extremely important point; that is, the question of the use of new drugs by the general practicing physician. I think that a good rule should be that they should be educated to the point where they should not be influenced by the brochures from pharmaceutical houses and they should not listen to the detail men. They should use these drugs in their practice only when there has been an adequate, thorough, and carefully controlled investigation.

Dr. Baer brought up the point of selection of patients. This is an important point, which I covered in the paper but to which I did not have time to refer today. Physician bias is an extremely important item in the selection of patients, and I will not enumerate all the various biases which can occur, but they are numerous. Therefore, what the investigator should do is to list the criteria; this should be done in a completely objective manner, and it should be checked by the statistician before he ever starts his study.

Changes in the Ten Commonest Dermatoses in Private Practice

A Comparison Between the Findings in 1930 and 1955

EDWARD F. CORSON, M.D.; HERBERT A. LUSCOMBE, M.D., and JOSEPH K. CORSON, M.D., Philadelphia

A comparison of the diagnoses of the 10 most commonly encountered skin diseases in private practice just prior to 1930 is made with an equal number of dermatoses in the 18 months preceding Dec. 1, 1955. Although but 3,419 cases are under consideration in each list, they may serve the purpose of stressing the diagnoses most frequently encountered. This knowledge may be useful for undergraduate teaching. Incidentally, the increase in the number of cases of contact dermatitis listed is pointed out.

A casual remark by a prominent dermatologist at a recent meeting was of more than passing interest when he said, "The undergraduate teaching of dermatology in *some* of our leading medical colleges is in a sad way." (Observe that "some" was the word used, not "all.") Whether true or not, it was the sort of challenge which should cause all teachers of the subject to appraise their methods and their scope. There are numerous successful plans on record. Note, for instance, Murrell's [1] sensible method of teaching undergraduates and Williams' [2] "Blueprint"—both valuable guides for dealing with the subject.

Over 25 years ago, when one of us (E. F. C.) was actively engaged in undergraduate teaching, it seemed desirable to determine the 10 commonest skin diseases so that stress could be laid on this group, affording the third- and fourth-year students better groundwork for diagnosing and treating the cases most likely to be encountered by them in practice. Ten was arbitrarily decided upon as the number to be employed, mainly because of ease of comparison with former tabulations. Of course, we dealt with the cases seen in the Philadelphia area—when the students scattered they might find an entirely different state of affairs in their chosen region—but that was our limitation.

Three thousand four hundred nineteen new cases were in the group tabulated in 1930. How that particular number was obtained is not now clearly recalled, but it probably represented the new cases admitted to private practice in the preceding two years—a number we fear too small to carry much weight from a statistical standpoint. Against that figure we have checked back the last 3,419 new private cases ending Dec. 1, 1955, of the three co-workers. The diagnoses in our tables comprise roughly 60% of the total number of cases reviewed.

The reason for writing this paper was that we felt that a change in the proportions had taken place in the last quarter century and that emphasis might be altered somewhat in undergraduate teaching. In Alden, Jones, and Nippert's [3] paper and the discussion that followed it, including information derived from private conversations with teachers of undergraduates in leading medical schools who were present at the session at which it was delivered, it was learned that in some instances only a limited number of dermatoses were presented in

Submitted for publication July 24, 1958.

Read before the 78th Annual Meeting of the American Dermatological Association, Inc., Sun Valley, Idaho, June 6, 1958.

detail to the student. To such instructors the relative incidence of the commoner diseases in our experience might be of interest, especially to those teachers in institutions where time for that purpose is very restricted.

Among the articles touching on this subject, Gilman,[4] Alderson and Reich,[5] Mintzer,[6] and Meyers[7] limited their coverage to students, high school or college, and therefore did not present an over-all picture of the dermatological field; Arena and Harris[8] and Tauber[9] dealt only with children. Goodman[10] and Sohrweide[11] computed their statistics for all ages, the last such article being published over 25 years ago.

A good many years ago this Association displayed considerable interest in the statistics of incidence of the various diseases of the skin. Annual reports made by the members were tabulated by Pollitzer, and the results have been published and reviewed by several additional writers.

In his table of "Published Statistics on Order of Incidence of Most Common Diseases of the Skin," Pollitzer[13] found eczema in number one position in all of the seven sources and acne next in frequency under six of the headings. While the contributions of Crocker,[15] Bulkeley,[16] Pollitzer,[13] and the New York Skin and Cancer Hospital[17] varied somewhat in the incidence of various diseases, scabies, psoriasis, seborrhea, impetigo, urticaria, dermatitis venenata, tinea, and alopecia were placed in about this order to complete the 10 commonest diagnoses.

Pollitzer pointed out that, as the years went by, the diagnoses were made by more and more experienced dermatologists and more reliance could be placed on their listings. In 1877, the first year covered, 32% of the cases were classed as eczema, but by the time of his first report, 1911, the incidence had fallen to 18.5%, as the large block of cases originally so designated had been split into different categories by increased diagnostic skill. He was surprised that no cases of scabies were reported by the Skin and Cancer Hospital in the year 1877-1878 but concluded that cases of that disease were erroneously included under eczema. Dermatitis venenata was in 11th place in his summary of the A. D. A. cases ending in 1911.

From our 1930 survey, responsibility for which lies upon one of us (E. F. C.), the following 10 diseases and their percentages are shown in the Table.

These diagnoses were those made for admission complaints. If two unrelated diseases were found at that first visit, as, for instance, acne vulgaris and a plantar wart, such a patient would be scored under two diagnoses, but if some complication arose later, such as a contact dermatitis from an ill-borne local medication or dermatitis from an allergy to a drug in course of treatment of the original dermatosis, that was not counted as an additional diagnosis.

Again, a motivating force for writing this paper was the impression we derived from day-to-day practice that we were seeing an increasing number of cases which we diagnosed as contact dermatitis. We have endeavored to avoid bias in favor of this diagnosis and were surprised to find it so predominant in our list.

The dermatitis venenata of 1930 (Table) was composed largely of cases resulting from contact with plants, dyes, or other chemicals and woods. In 1955 (Table), the number of cases of contact dermatitis was especially swelled by two factors: first, by cases from the old eczema group which

Data from 1930 and 1955 Surveys

1930		1955	
Tinea (all types)	0.1299	Contact dermatitis	0.111
Acne vulgaris	0.0886	Acne vulgaris	0.070
Eczema	0.0819	Eczematous dermatitis	0.0655
Verruca	0.0716		
Seborrheic dermatitis	0.058	Seborrheic dermatitis	0.064
Impetigo	0.0470	Verruca	0.0615
Psoriasis	0.0339	Tinea (all types)	0.0610
Scabies	0.0318	Nevi (broadly classed)	0.059
Cancer (cutaneous)	0.0312	Keratosis (all types)	0.055
Dermatitis venenata	0.0310	Psoriasis	0.044
		Cancer (cutaneous)	0.042

increased diagnostic ability has allowed us to define etiologically as being due to various local causes, and, second, the many new allergens in industry and in everyday use. This last is probably the chief reason for the increase. As a consequence, our figures rose from 3.10% for dermatitis venenata of 1930 to 11.1% for the contact dermatitis of 1955, which is given first place in its list. On the other hand, tinea, our number one in 1930, dropped to sixth in 1955. It is of interest to recall Goodman's [12] article of 1931 entitled, "Tinea, the Second Most Prevalent Disease of the Skin," indicating that our figures were not much out of line with his findings about the same time. We hesitate to believe that the drop in number in this group is due to an actual decrease in ringworm cases, for pathogenic fungi are still widely distributed. Perhaps the well-advertised proprietary preparations sold over the counter have allowed more patients to treat themselves successfully and avoid visits to the dermatologist.

Seborrheic dermatitis rose from fifth to fourth place. Acne vulgaris held a fairly level position. With our system of tabulating more than one original finding it is likely that some of the patients appeared under both acne and seborrheic dermatitis when the latter was severe. The eczema of 1930 may readily include many cases of contact dermatitis which, then titled dermatitis venenata, barely reached inclusion in the first 10%. The most outstanding change in the two lists is the spectacular advance of contact dermatitis by 1955.

Warts held a fairly steady position, as did psoriasis and cancer, but impetigo and scabies did not qualify in the later table. Better personal and public hygiene undoubtedly account for this last change. Our private practices never included a high percentage of syphilis, and in 1955 that disease had shrunk in frequency nearly to zero. Nevi were seen in increasing numbers. Present-day medical education of the public, through newspapers and magazines, has made readers so aware of every small mass on the skin that the opinion of the physician is frequently sought in this connection. Today this subject has become a necessary item in the teaching of dermatology to the undergraduate.

It is very difficult to compare the eczema of 1930 (Table) with the various eczematoid dermatitides of today's nomenclature, and we endeavor only to attempt to point out the increase of the cases we now regard as contact dermatitis from among the number of the old classification. In addition, it would seem to be fairly apparent that with the unrecognized cases in that group we have acquired through our changed habits, occupations, and mode of life many new instances and types of contact dermatitis. In the eczematous dermatitis group of the 1955 table we have included atopic dermatitis, neurodermatitis, nummular eczema, and the clinically similar eruptions which may be due to allergies to foods, drugs, bacteria, viruses, and fungi.

Summary

A comparison of the diagnoses of the 10 most commonly encountered skin diseases in private practice in 1930 is made with an equal number of dermatoses in 1955. This is intended as an aid to those who are limited to a few diseases in their instruction to undergraduates and who wish to stress the commoner conditions in the limited time at their disposal. Incidentally, the considerable increase in the number of cases of contact dermatitis is pointed out.

136 S. 16th St. (2).

REFERENCES

1. Murrell, T. W.: A Suggested Plan for Undergraduate Dermatological Teaching, South. M. J. 47:379 (April) 1954.

2. Williams, D. H.: A "Blueprint" for the Teaching of Undergraduate Dermatology, A. M. A. Arch. Dermat. 75:217 (March) 1957.

3. Alden, H. S.; Jones, J. W., and Nippert, P. H.: Undergraduate Instruction in Dermatology, A. M. A. Arch. Dermat. & Syph. 69:1-10 (Jan.) 1954.

4. Gilman, R. L.: Incidence of Skin Diseases in Student Health Service, Am. J. M. Sc. 188:268 (Aug.) 1934.

5. Alderson, H. E., and Reich, A.: Incidence of Dermatoses in Student Health Service, Arch. Dermat. & Syph. 36:57 (July) 1937.

6. Mintzer, I. J.: Frequency of Certain Dermatoses in High School Girls, Arch. Dermat. & Syph. 42:475 (Sept.) 1940.

7. Meyers, J.: Physical Findings in New York City Continuation School Boys, Am. J. Pub. Health 21:615 (June) 1931.

8. Arena, J. M.; and Harris, R. R.: Frequency and Distribution of Diseases in Children, South. Med. & Surg. 97:520 (Sept.) 1935.

9. Tauber, E. B.: Diseases of the Skin: Cases Commonly Seen in Children, Arch. Pediat. 47:428 (July) 1930.

10. Goodman, H.: Statistics of the 10 Most Common Skin Diseases, Arch. Dermat. & Syph. 20:186 (Aug.) 1929.

11. Sohrweide, A. W.: Recent Changes in Dermatologic Diagnosis, Arch. Dermat. & Syph. 30:260 (Aug.) 1934.

12. Goodman, H.: Tinea, the Second Most Prevalent Disease of the Skin, Arch. Dermat. & Syph. 23:872 (May) 1931.

13. Pollitzer, S.: Report of the Committee on Statistics of the American Dermatological Association, J. Cutan. Dis. 32:312 (April) 1914.

14. Pollitzer, S.: Statistical Report of the ADA for the year 1916, J. Cutan. Dis. 36:294 (May) 1918.

15. Crocker, H. R.: Diseases of the Skin, Philadelphia, The Blakiston Company (division of McGraw-Hill Book Company, Inc.), 1903, p. 1401.

16. Bulkeley, L. D.: Diseases of the Skin, New York, Paul B. Hoeber, Inc., 1898, p. 41.

17. New York Skin and Cancer Hospital Annual Reports.

ABSTRACT OF DISCUSSION

Dr. George H. Curtis, Cleveland: I congratulate Dr. Corson and his colleagues on their comprehensive paper. It is ideally short but provides much food for thought in both the teaching and the future of dermatology. It was most interesting to attempt to draw some comparison between the common dermatoses seen in independent private practice and group practice.

For the sake of brevity, only the list of diseases of 1955 are presented.

Corson et al.	%
Contact dermatitis	11.1
Acne vulgaris	7.0
Eczematous dermatitis	6.55
Seborrheic dermatitis	6.4
Verruca	6.15
Tinea	6.10
Nevi	5.9
Keratoses	5.5
Psoriasis	4.4
Cancer	4.2
Cleveland Clinic	%
Neurodermatitis circumscripta (incl. anogenital pruritus)	9.41
Tinea	8.79
Pyogenic infections	7.63
Seborrheic dermatitis	6.5
Contact dermatitis	6.3
Nevi	6.2
Acne vulgaris	5.2
Atopic dermatitis	4.0
Keratoses	3.7
Psoriasis	3.4

Dr. Corson's list comprises the 10 commonest diseases among 3,419 new diagnoses. The list from the Cleveland Clinic comes from 4,833 new diagnoses. Dr. Corson's has included skin cancer and eczematous dermatitis, which are not present in ours. I can only postulate that meteorologic conditions may play a role in the incidence of cancer, since the Great Lakes region is considered one of the areas in the United States having the least amount of year-around sunshine. On the other hand, if we group the diseases mentioned by Dr. Corson under eczematous dermatitis, then skin cancer enters our list, as we had 130 cases in 1955. I believe that another factor in maintaining skin cancer as a common disease is the ever-increasing age of our population.

Our statistical department more or less forces us to follow as closely as possible the Standard Nomenclature of Diseases and Operations; thus, we may more accurately separate members of the various eczematous dermatoses. I think that we see a large number of cases in the neurodermatitis, tinea, pyogenic infection of the skin, and nevus groups because our sections on proctology, allergy, diabetes, pediatrics, peripheral vascular diseases, general medicine, surgery, and so forth funnel them to us. We probably see fewer cases of acne because we do not maintain Saturday office hours.

Another disease which would enter the Cleveland Clinic list if we lumped the neurodermatoses and eczematoses together is syphilis, for in 1955 we had 155 cases which we had to study from the standpoint of positive serologic reactions.

It is noteworthy that in Dr. Corson's and our lists the diseases are of the same order of frequency, and compare on the whole reasonably with other published data. These diseases comprise about 60% of his series and 61% of ours. As the authors indicated, there are between 10 or 15 common diseases that may well form a nucleus for undergraduates and teaching of interns, for the

diseases seem to maintain their frequency throughout the United States. Furthermore, the great majority of these diseases probably are first seen by physicians other than dermatologists. Our statistician informs me that in the new AMA Standard Nomenclature, dermatitis medicamentosa and contact dermatitis are to be assigned to the same index number. Hence, drug eruptions will enter the lists in the future.

As medicine increases in depth of knowledge, I see dermatology receding from a clear-cut specialty, which, as late as twenty years ago, seemed more concerned with clinical descriptions, but now seems to be returning more and more to internal medicine. Symbolically speaking, dermatologists today are increasingly driven to resurrect their stethoscopes. I think this is apparent from the changes taking place in dermatologic literature, the changes in teaching courses of the American Academy of Dermatology, the changes in the syllabus on training of the American Board of Dermatology, and it was brought into sharp focus to me in the study of the diagnoses made in the clinic in 1935 and 1955.

Along with the advances in dermatology, there is the increasing pressure on dermatologists to obtain wide, comprehensive statistical information, and to make searching assays of many skin diseases and therapeutic regimens. The questionnaires received by us in recent years are increasingly numerous and more and more demanding in all phases of the diseases, including an expanding amount of laboratory data. Recently, I received a questionnaire about which I had to consult our statistician. We concluded that it would take about six months to obtain probably more than 1,000 of our medical charts from which to cull the necessary data to answer the more than 20 questions.

This brings up a suggestion for serious consideration in our dermatological organizations: that a central registry be established to maintain all diagnoses of skin diseases and correlated data. The information can be forwarded by all dermatologists and/or designated key institutions throughout the country. The central registry may, in turn, supply all the necessary information for scientific papers and questionnaires of such broad scope.

DR. LEONARD F. WEBER, Chicago: Dr. Corson's paper interested me, as it recalled my introduction to dermatology in Dr. Pusey's office, between my junior and senior years in medical school. It was one of my duties to keep an orderly collection of the number of new cases and the diagnosis in each case seen in his private practice. I hasten to add that for many years every member of the American Dermatological Association was requested by this Association to keep such a record for their use. His file had its beginning in the early 1900's. His statistical study was discontinued in 1933, when our many cases of occupational dermatoses confused the system of keeping an accurate record of common and uncommon dermatoses.

I recall the records of the common dermatoses seen in his practice from about 1903 to 1920. Cutaneous cancer headed his list of common dermatoses. He was a pioneer in the roentgen therapy of cancer and had first call in the treatment of this disease until about 1920. Then, radiologists in some of the hospitals treated cancer, particularly cutaneous cancer. This caused a gradual decrease in the number of cases of cutaneous cancer in his practice from 1920 to 1933.

Chromoblastomycosis Treated with Local Infiltration of Amphotericin B Solution

MAURICE J. COSTELLO, M.D.; CHARLES P. DeFEO JR., M.D., and M. L. LITTMAN, M.D., Ph.D., New York

Chromoblastomycosis is a mycotic infection limited to the exposed cutaneous and subcutaneous tissues of man. It occurs in tropical and subtropical regions, particularly in Central, South, and North America. The first case recognized in the United States occurred in Boston, where it was reported in 1915 by C. G. Lane.[1] Occasional cases have been reported since then by Moore and Mapother,[2] Weidman and Rosenthal,[3] Binford et al.,[4] Lewis et al.,[5] and Conway and Berkeley.[6] J. K. Howles et al.[7] described nine cases in Louisiana in a single report. The majority of infections appears in male laborers, presumably because of their contact with soil and wood and to the frequency with which their minor wounds become contaminated during work. Chromoblastomycosis is not a systemic infection. It does not involve internal organs or bone.

Chromoblastomycosis has been treated by surgical excision, electrosurgery, potassium iodide by mouth, sodium iodide intravenously,[8] iontophoresis with copper sulfate,[9] and subcutaneous injections with calciferol (vitamin D_2).[10,11] Small involved areas of the skin may be surgically excised, but this method may require a protracted period of hospitalization, especially if the lesions are numerous and require plastic repair. Since amphotericin B * has been used with success in the therapy of the deep mycoses, such as coccidioidomycosis [12,13] and North American blastomycosis,[14] a trial of this new antibiotic was considered for the treatment of this case of chromoblastomycosis. One of the limitations of amphotericin B in the therapy of chromoblastomycosis is the relatively high degree of resistance to the drug by the causative organism of the disease. Gold and co-workers [15] reported that the minimal inhibitory concentration (MIC) of all three species, Phialophora verrucosa, Hormodendrum compactum, and Hormodendrum pedrosoi, was greater than 40μg. per milliliter in vitro. The second limitation of the use of amphotericin B is the low blood serum levels obtained with intravenous administration of the antibiotic. For instance, the maximum intravenous dose of amphotericin B tolerated by humans is 1.0 to 1.5 mg. per kilogram per day, which produces a blood level of antibiotic no greater than 1.8μg. per milliliter.[13] Since amphotericin B was reported to be well tolerated locally in intra-articular and intrathoracic sites [13] and high local concentrations of the antibiotic were obtained, a therapeutic trial of amphotericin B by subcutaneous injections was undertaken in a patient with chromoblastomycosis.

Report of a Case

A 47-year-old Negro handyman, born in Georgia, accidentally injured his right ankle with an ax, in 1950, while chopping wood in Salem, a southern New Jersey community. A wound appeared on the medial aspect of the right ankle, which did not heal. A raised cutaneous lesion developed. As the years progressed, this lesion increased in size peripherally while its central area became verrucoid and encrusted. In September, 1957, as a result of a routine preemployment physical examination at

Submitted for publication July 3, 1958.

Read before the 78th Annual Meeting of the American Dermatological Association, Inc., Sun Valley, Idaho, June 5, 1958.

From Department of Dermatology and Medicine, Lenox Hill Hospital (Dr. Costello and Dr. DeFeo). Research Associate, Department of Microbiology Mount Sinai Hospital (Dr. Littman).

* E. R. Squibb & Sons, Division of Olin Mathieson Chemical Corporation.

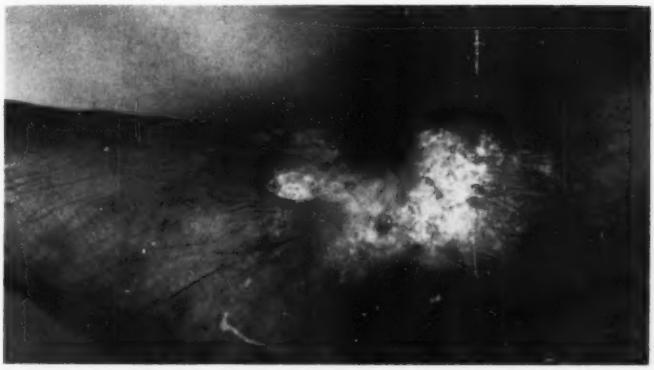


Fig. 1.—Medial aspect of the right ankle before therapy, showing verrucoid scaling character of the lesion.

Lenox Hill Hospital, New York City, the patient was found to have an abnormal roentgenogram of the lungs. He was hospitalized for diagnostic studies and treatment.

History.—History revealed that the patient had engaged in numerous occupations along the eastern seaboard from Florida to New York. He had also spent one day in Cuba, 20 years previously. During the previous five years, he had sought lighter work because of increasing exertional dyspnea. A history of exposure to a known case of tuberculosis was elicited.

Physical Examination.—Physical examination revealed a well-nourished, Negro man with bilateral interstitial keratitis which was caused by congenital syphilis. On the medial aspect of the right foot and ankle there was an irregularly outlined, verrucoid, scaly, crusted, and painless lesion of the skin and subcutaneous tissues. The lesion measured 6 by 10 cm. (Fig. 1). The center of the involved area was studded with several smooth, lilac-colored, truncated, and infiltrated pea-sized nodules, surrounded by an area of hyperpigmentation.

Roentgenograms of the lungs revealed bilateral hilar enlargement and a diffuse mottled infiltration of both lung fields, mostly of the upper lobes, which was consistent with a diagnosis of either sarcoidosis or pneumoconiosis. Roentgenograms of the hands showed a cystic lesion of the bone of the distal phalanx of the left fourth finger. Roentgenograms of the bone beneath the cutaneous lesion of the right ankle revealed a pressure phenomenon, causing slight erosion of the cortex but no evidence of osteomyelitis.

Laboratory Data.—Hemograms and urinalyses were normal. Blood sedimentation rate was 87 mm. in one hour (Wintrobe). Total serum protein was 6.6 gm. %, and albumin-globulin ratio was 2.8/3.8. Serum electrophoresis showed a decrease in albumin and an elevation in γ-globulin components. Serum calcium was 10.8 mg. %. Massini and Kline serologic tests for syphilis were negative, but the Treponema pallidum immobilization test was positive. Nine sputum specimens and two gastric-fluid cultures were negative for tubercle bacilli and pathogenic fungi. Histologic examination of the liver obtained by needle biopsy revealed normal liver architecture.

Biopsy.—Biopsy of the verrucoid lesion on the right ankle revealed stratified squamous epithelium with pseudoepitheliomatous changes. Extensive areas of necrosis were present in the underlying dermis. The subcutaneous tissue was heavily infiltrated with lymphocytes and contained numerous multinucleated giant cells. Scattered throughout the areas of infiltration were occasional spherical, yellowish-brown, septate, fungal sclerotic cells found either free or in clusters or within the giant cells. The tissue reaction, in addition to the presence of the characteristic organisms, was diagnostic of chromoblastomycosis.

Culture.—Culture of the biopsy specimen on Sabouraud's dextrose and Littman oxgall agars revealed a slowly growing, black, filamentous mold, which was identified as H. pedrosoi. Both Hormodendrum and Phialophora types of conidia formation were observed in potato-dextrose slide cultures.

In Vitro Sensitivity Tests.—Minimal inhibitory concentration of amphotericin B for the strain isolated from the patient was 35μg. per milliliter after an incubation period of five days at 20 C in Penassay broth (Difco) containing 1% glucose. The MIC value increased to 45μg. per milliliter after nine days' incubation, and it was unchanged by addition to the medium of 10% sterile horse serum. It was also observed that 1% aqueous procaine solution, with 0.5% chlorbutanol as preservative, was fungistatic and fungicidal for H. pedrosoi when 1 ml. of procaine was added to 9 ml. of culture medium (0.1% concentration or 1,000μg. per milliliter of procaine).

Skin and Serologic Tests.—Skin tests with tuberculin (PPD), histoplasmin, coccidioidin, and blastomycin were negative. Two Kveim tests, performed in September, 1957, and February, 1958, with different antigens were negative in situ and

on histological examination of excised skin. An intradermal injection of 0.1 ml. of a sterile saline extract of the ground autogenous Hormodendrum culture caused erythema and induration in the patient's skin within 48 hours, which persisted for 10 days. The same antigen failed to elicit a reaction in several normal persons. Control injections of saline were negative. Precipitin test of patient's serum with a saline extract of this autogenous culture was negative.

Treatment with Amphotericin B.—A series of subcutaneous injections of procaine-amphotericin B, infiltrated beneath the ankle lesion, was made weekly or biweekly for a total of eight injections, the frequency of the injections being determined by the intensity and subsidence of the local reaction after each injection. Amphotericin B, 50 mg., was dissolved in 10 ml. of 2% aqueous solution of procaine to give an amphotericin B concentration of 5 mg. per milliliter, or 5,000μg. per milliliter. An average single subcutaneous injection of procaine-amphotericin B solution was 7 ml., although it varied from 4 to 9 ml. (20 to 45 mg.). During a period of 12 weeks, a total of 49 ml. was infiltrated beneath the infected skin for a total of 245 mg. of amphotericin B. The verrucoid and friable nature of the affected skin permitted some of the injected procaine-amphotericin B solution to leak out of the tissues, but the loss was minimal, estimated to be not more than 5 ml. of the total volume injected. Procaine in 2% solution, rather than 1%, was employed as a diluent for amphotericin B in order to diminish the pain produced by the injection of the antibiotic.

After each subcutaneous injection of procaine-amphotericin B solution, a small portion of the injected diseased verrucoid tissue sloughed away within two to five days. This was followed by reepithelization. Subcutaneous injection of the same concentration of procaine-amphotericin B in the contralateral, normal ankle caused some discomfort, mild erythema, and edema 48 hours later, which subsided in a few days. Sloughing of the normal skin did not occur. Because of the discomfort caused by the injection and the slow healing of the chromoblastomycotic lesion after each injection, procaine-amphotericin B was administered every seven days for seven doses. On one occasion an overdose of 40 mg. of amphotericin B (8.2 mg. per milliliter) was inadvertently injected beneath the skin. A painful local reaction occurred with erythema and edema. A systemic reaction with chills also occurred, as well as a mild enlargement of the right inguinal lymph node. This reaction began to subside and was complete within 48 hours. After a total of eight injections of procaine-amphotericin B had been administered over a period of 12 weeks, the thickened chromoblastomycotic area gradually diminished to the level of the surrounding skin. The infected area healed with progressive replacement of soft scar tissue and occurred coincident with amphotericin B therapy. At the end of treatment the clinical evidence of infection of the skin appeared to be completely resolved (Fig. 2).

Biopsy of the healed lesion showed resolution of the disease, with disappearance of the granulomatous reaction and replacement by fibroblastic scar tissue formation. Although a Gridley stain revealed a few fungus cells, four cultures of the biopsied material failed to show growth of fungi, indicating their lack of viability.

Comment

Intravenous administration of amphotericin B is of limited value for the therapy

Fig. 2.—Involution of the lesion after eight subcutaneous injections with amphotericin B.

Fig. 3.—Close-up of the same area shown in Figure 1.

of chromoblastomycosis because of the low attainable serum levels of the antibiotic (8.2μg. per milliliter), compared with the concentration required to inhibit the organism (35μg. per milliliter). Fortunately, the nondisseminated and localized nature of chromoblastomycotic lesions permits direct local subcutaneous injection of the antibiotic. Such injections of amphotericin B in doses of 20 to 35 mg. (20,000μg. to 35,000μg.) in 2% procaine were tolerated when injected subcutaneously in normal sites. When injected beneath a chromoblastomycotic lesion, however, procaine-amphotericin B caused sloughing of the lesions in the area in which the injection was given and eventual healing of the skin. The high concentration of amphotericin B in the subcutaneous tissue produced by the above injected doses certainly exceeds the concentration required to inhibit H. pedrosoi in culture. A single dose of 40 mg. (8.2 mg. per milliliter) was considered to be above the optimal dose, since it caused severe local tissue reaction and mild systemic reaction. In view of the hypersensitivity of certain

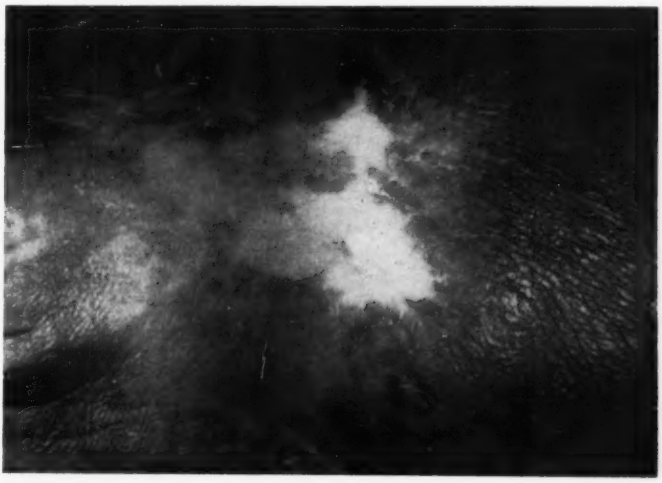


Fig. 4.—Close-up of the involved area at the completion of local injections of amphotericin B. Flat smooth scar now present.

Fig. 5. — Biopsy specimen shows pseudoepitheliomatous hyperplasia with replacement of the normal architecture by granulomatous tissue response. Hematoxylin and eosin; reduced approximately 10% from mag. × 48.3.

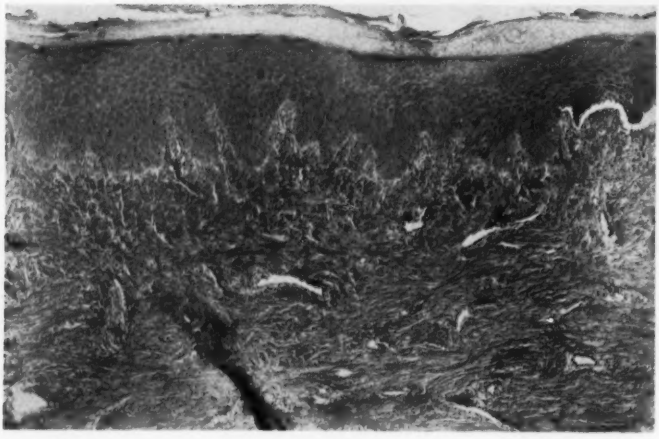


Fig. 6.—Repeat biopsy specimen from the same area of lesion after 12 weeks and eight local injections of amphotericin B, showing replacement of the granulomatous tissue reaction with fibrosis and small round-cell infiltrate especially marked in the subepidermal region. Hematoxylin and eosin; reduced 40% from mag. × 87.

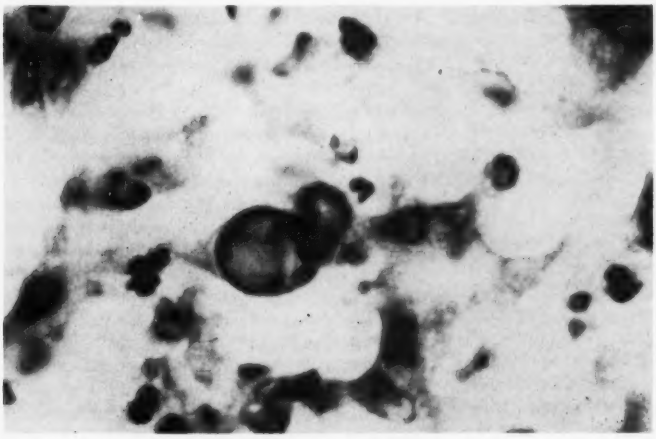


Fig. 7.—Large septate body with thick wall is shown surrounded by small round cells and polymorphonuclear leukocytes. Hematoxylin and eosin; reduced 40% from mag. × 617.

persons to procaine, preliminary skin testing is necessary. Care should also be exercised not to introduce the procaine-amphotericin B solution intravenously, since both drugs could give rise to severe reactions. The toxic manifestations of amphotericin B administered intravenously have been described by one of us (M. L. L.).[13]

Laboratory tests consistently failed to establish a diagnosis of pulmonary tuberculosis. Sputum examinations consistently failed to demonstrate Hormodendrum. The pulmonary disease most likely represents sarcoidosis.

Summary

A Negro patient with chromoblastomycosis of the ankle, caused by Hormodendrum pedrosoi, was treated for the first time with a series of local subcutaneous injections of amphotericin B dissolved in 2% procaine, with favorable clinical response. After eight injections had been administered over a period of 12 weeks, clinical resolution of the infected area occurred. Follow-up of the patient and further clinical trials of procaine-amphotericin B for chromoblastomycosis are necessary to evaluate fully the effectiveness of the combined medication in the treatment of this fungus disease.

140 E. 54th St. (22).

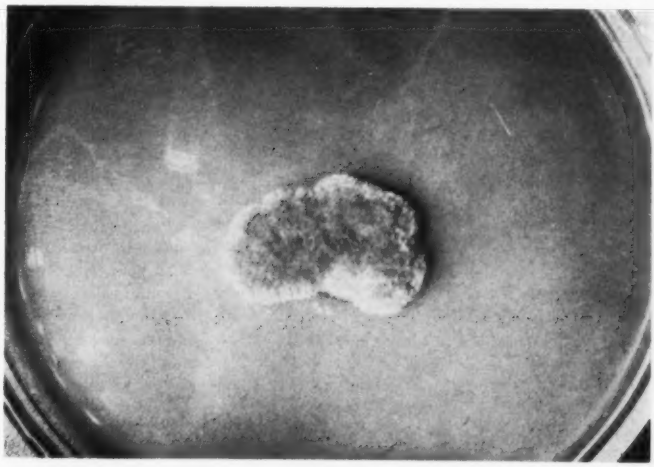


Fig. 8.—One-month old culture shows furry mouse-colored colony growing on Sabouraud's medium.

REFERENCES

1. Lane, C. G.: A Cutaneous Lesion Caused by a New Fungus (Phialophora Verrucosa), J. Cutan. Dis. 33:840-846, 1915.

2. Moore, M., and Mapother, P.: Chromomycosis of the Face: Report of a Case and a Study of the Causative Organism, Phialophora Verrucosa, Arch. Dermat. & Syph. 41:42-54, 1940.

3. Weidman, F. D., and Rosenthal, L. H.: Chromoblastomycosis: A New and Important Blastomycosis in North America: Report of a Case in Philadelphia, Arch. Dermat. & Syph. 43: 62-84, 1941.

4. Binford, C. H.; Hess, G., and Emmons, C. W.: Chromoblastomycosis: Report of a Case from Continental United States and Discussion of the Classification of the Causative Fungus, Arch. Dermat. & Syph. 49:398-402, 1944.

5. Lewis, G. M.; Hopper, M. E.; Sachs, W.; Cormia, F. E., and Potelunas, C. B.: Mycetoma-like Chromoblastomycosis Affecting the Hand: Further Findings and Comparative Mycologic Studies, J. Invest. Dermat. 10:155-168, 1948.

6. Conway, H., and Berkeley, W.: Chromoblastomycosis (Mycetoma Form) Treated by Surgical Excision: Correction of Defect by Cross Leg Pedicled Flap, A. M. A. Arch. Dermat. & Syph. 66:695-702, 1952.

7. Howles, J. K.; Kennedy, C. B.; Garvin, W. H.; Brueck, J. W., and Buddingh, G. J.: Chromoblastomycosis: Report of 9 Cases from a Single Area in Louisiana, A. M. A. Arch. Dermat. & Syph. 69:83-90, 1954.

8. Carrión, A. L.: Yeastlike Dematiaceous Fungi Infecting the Human Skin: Special Reference to So-Called Hormiscium Dermatitidis, Arch. Dermat. & Syph. 61:996-1009, 1950.

9. Martin, D. S.; Baker, R. D., and Conant, N. F.: A Case of Verrucous Dermatitis Caused by Hormodendrum Pedrosoi (Chromoblastomycosis) in North Carolina, Am. J. Trop. Med. 16:593-620, 1936.

10. Bopp, C.: Tratamento da cromoblastomicose pelo Calciferol (Monograph), 1957.

11. Bonilla, E.: Treatment of Chromoblastomycosis with Calciferol: Report of 3 Cases, A. M. A. Arch. Dermat. & Syph. 70:665-667, 1954.

12. Littman, M. L.: Preliminary Observations on the Intravenous Use of Amphotericin B, and Antifungal Antibiotic, in the Therapy of Acute and Chronic Coccidioidal Osteomyelitis, Conference on Coccidioidomycosis: U. S. Department of Health, Education, and Welfare and Arizona State Health Department, Phoenix, Ariz., Feb. 11-13, 1957, pp. 86-94.

13. Littman, M. L.; Horowitz, P. L., and Swadey, J. G.: Coccidoidomycosis and its Treatment with Amphotericin B, Am. J. Med. 24:568-592, 1958.

14. Harrell, E. R., and Curtis, A. C.: The Treatment of North American Blastomycosis with Amphotericin B, A. M. A. Arch. Dermat. 76:561-569, 1957.

15. Gold, W.; Stout, H. A.; Pagano, J. F., and Donovick, R.: Amphotericins A and B, Antifungal Antibiotics Produced by a Streptomycete: I. In Vitro Studies, Antibiotics Ann., p. 579-586, 1955-1956.

16. Berger, L.; Beaudry, M., and Gaumond, E.: Chromoblastomycosis Due to a New Species of Fungus, Canad. M. A. J. 53:138-143, 1945.

17. Burns, R. E.: Chromoblastomycosis in a Canadian Airman Serving in Ceylon, Canad. M. A. J. 63:595-596, 1950.

18. Carrión, A. L.: Chromoblastomycosis, Ann. New York Acad. Sc. 50:1255-1282, 1950.

19. Azulay, R. D.: Experimental Chromoblastomycosis in Man, J. Invest. Dermat. 19:307-309, 1952.

20. Barwasser, N. C.: Chromoblastomycosis: Thirteenth Reported Case in the United States, J. A. M. A. 153:556, 1953.

21. LeVan, N. E.: Chromoblastomycosis, California Med. 80:468-470, 1954.

22. Kaess, K. V.; Reberger, C. C., and Sloss, P. T.: Chromoblastomycosis: Laboratory Observations on the Causative Organism, U. S. Armed Forces M. J. 6:739-746, 1955.

23. Jacobson, F. W.; Clearkin, F. P., and Annamunthodo, H.: Chromomycosis: Report of 4 More Cases in Jamaica, West Indian M. J. 3:153-158, 1954.

24. Procknow, J. J., and Loosli, C. G.: Treatment of the Deep Mycoses, A. M. A. Arch. Int. Med. 101:765-802, 1958.

25. Velutini, L. A., and Borelli, D.: Un Caso de cromomicosis del tronco por Fonsecaea pedrosi, Dermat. venezol. 1:95, 1957.

ABSTRACT OF DISCUSSION

DR. THOMAS H. STERNBERG, Los Angeles: First, I want to congratulate Dr. Costello on a very excellent presentation. My associates, Dr. Victor Newcomer and Dr. Edwin Wright, have been working with amphotericin B for a number of years, and we feel that this presentation not only is a real contribution in terms of the treatment of a very difficult fungus disease but also that it opens up areas of use for amphotericin B which may go a way beyond just the disease of chromoblastomycosis.

Amphotericin B is a very interesting drug because it is possibly the only antifungal antibiotic that can be administered topically, subcutaneously, and intravenously. During the past three or four years we have had rather a lot of experience with it in a series of deep fungus infections which I should like to mention briefly.

The drug is a member of a large family of polyene antifungal agents, which includes nystatin, Rimocidin, Candicidin, Ascosin, Trichomycin, and Filipin. It has been given a tentative formula of $C_{46}H_{73}NO_{20}$. In vitro it inhibits a wide variety of pathogenic and nonpathogenic fungi.

The dosage that we have adopted is to begin with 10 mg. daily and then build up to 50 or 100 mg. The patients frequently have chills and fever but do not consider them a contraindication to continuing therapy. Other reactions include severe nausea with vomiting and chest pain. This may require a lowering of the dosage. Several patients have developed a rising BUN and a fall in hemoglobin. In these instances we have stopped therapy, and in each case these findings have returned to normal.

We have treated 20 patients with a variety of deep fungus infections, as follows:

Diagnosis	Patients, No.
Coccidioidal meningitis	5
Disseminated coccidioidomycosis	8
Aspergillosis	1
Candida parakrusei of the eyeball	1
Cryptococcal meningitis	4
Madura foot (Monosporium apiospermum)	1

Some were almost moribund at the time we instituted therapy, and a number have since died, but we have had some excellent results. Coccidioidal meningitis in our experience has been almost invariably fatal, but we have two patients now who are doing well on daily amphotericin B. Their spinal fluid findings are returning to normal, and mental symptoms and physical or neurological signs are decreasing. There are two who appear to be just hanging on. One patient is dead. The patient with pulmonary aspergillosis has done remarkably well. The Candida infection of the eye has healed. Two of the patients with cryptococcal meningitis are now dead. One is still alive but not doing very well. A fourth patient has exhibited a most dramatic and immediate effect from the beginning of amphotericin B therapy. As far as we can tell he is completely well and spinal fluid and cultures are negative.

In general, amphotericin B has proved to be a very effective and even life-saving drug in certain patients with deep fungus diseases. Dr. Costello has opened up a new method of application of this drug which may prove to be most valuable.

DR. V. PARDO-CASTELLO, Havana, Cuba: Dr. Costello has certainly made a definite contribution to the treatment of chromoblastomycosis by the use of amphotericin B. I believe that this is going to be one of the most successful agents used in the treatment of this recalcitrant skin condition.

However, I want to call attention to several points in the histopathology of this condition which may alter the usefulness of amphotericin B in its treatment. Most of the cases of chromoblastomycosis occur in people (belonging to the colored races) of the working class or in people who work gathering the crops or in any other way in the rural sections of the tropics. Most of them do not come to the physician as soon as the condition appears but go on for months and sometimes for years before they seek medical aid. Therefore, the reaction of the tissues to the presence of this fungus is of the greatest importance in the creation of the different clinical forms and in the accessibility of the fungus to the medicament that may be used.

We have been classifying these cases into the granulomatous type, with more or less infiltration or ulceration, as you see in the case presented by Dr. Costello: the dystrophic type, with a great amount of hypertrophy, so that there is sometimes even keloidal scarring and, in some cases, atrophy of the skin after a number of years, where self-healing has taken place while the fungus condition continues to spread peripherally.

We have found, of course, that the classical treatment with iodides, either by intravenous injection or by mouth, has been successful in the early cases, cases in which there is still a very small amount of tissue reaction in the form of fibrosis. Once the fibrosis is established, particularly in the colored races, where the production of keloidal scarring is very common, the disease may become completely intractable and may affect a whole limb, leg, and thigh or the arm, the hand, and forearm, and so the only remedy in these cases is surgical amputation of the affected part. Any other treatment will absolutely fail in the complete eradication of the disease, even after months and years of treatment.

One advance in the treatment of chromoblastomycosis was made recently by the administration of calciferol (vitamin D_2), either by mouth in alcoholic solution, by intramuscular injection, or orally in the form of tablets. Fifty thousand units twice a week is a sufficient amount of this vitamin, combined with iodides intravenously or by mouth, to produce slowly and gradually resolution of the lesions, provided there is not a great amount of fibrosis.

There is another clinical type of chromoblastomycosis in which this treatment presented by Dr. Costello might be very useful, the lymphangitic type. That is an unusual occurrence, with small lesions along the course of the lymphatic vessels, three or four or more small abscesses, and the formation in time of the verrucous type of lesions. In those cases, the administration of iodides in large doses has been very successful, and I think that amphotericin B would be, too, locally injected.

As to the systemic administration of amphotericin B, I have seen such disagreeable reactions that only in the most serious cases of systemic mycosis, I think, should it be used.

DR. JAMES LEWIS PIPKIN, San Antonio, Texas: In this particular instance, where there is so much scarring and fibrosis, we all readily appreciate the difficulty that this drug would experience in getting to the source of the trouble, when given intravenously. Our experience with the use of amphotericin B in the deep mycosis has been very limited, and the situations confronting us have been entirely different. We recently had a primary cutaneous infection of histoplasmosis that presented a massive granuloma of the forehead, and this particular solitary lesion was very soft and richly supplied by blood and responded very readily to the intravenous use of amphotericin B, in the dose recommended by Dr. Curtis and Dr. Harrell. We experienced very little systemic reaction, and the lesion responded rapidly, the massive granuloma disappearing with a course of 20 intravenous injections over a 24-day period.

The reactions experienced by us would certainly not contraindicate the intravenous use. We did experience some increase in the BUN, and on two occasions we had to rest two days, but the abnormal blood chemistry findings quickly returned to normal. There was a slight elevation of temperature, but this was not too objectionable.

DR. EVERETT R. HARRELL, Ann Arbor, Mich.: To my knowledge Dr. Costello has just reported the first case of chromoblastomycosis successfully treated with amphotericin B. I want to congratulate him on this report. I do not think that it would be logical to treat most of the other deep mycoses by the local instillation of this antibiotic, since the cutaneous lesions of North American blastomycosis, coccidioidomycosis, histoplasmosis, and cryptococcosis nearly always represent just the cutaneous expression of a true systemic disease. It is my feeling that, with the exception of isolated instances of primary inoculation, these fungus diseases are acquired by pulmonary inhalation. The intravenous use of amphotericin would, therefore, be preferable to the local instillation of this antibiotic.

Some of you may recall that last year I reported on our preliminary results of the treatment of North American blastomycosis with amphotericin B administered intravenously. We recorded five cases at that time. We have now treated a total of seven cases of this disease with this fungicidal antibiotic. Six of these seven patients are alive and well and exhibit no manifestations of activity whatsoever. The seventh patient has had two relapses after therapy. This patient has a widespread cavitary form of the disease. His relapses have been documented by finding the organism in his sputum. He has now had a total of 3.5 gm. of amphotericin B. His lung disease is so extensive that the thoracic surgeons have felt him to be inoperable. I am dubious that we can expect a cure of his mycotic infection with any form of chemotherapy, no matter how fungicidal it might be. We have also treated two cases of histoplasmosis. One of these was a 5-month-old boy who was admitted with the typical clinical findings of progressive disseminated histoplasmosis. The organisms were recovered from bone marrow aspiration. As his disease progressed, his positive histoplasmin skin test became negative and he developed a significant complement-fixing antibody titer. He was treated with amphotericin B administered by slow intravenous drip in a dosage of 1 mg. per kilogram per day for a total of 20 days. His response to the antibiotic was very dramatic. Six months have now elapsed since the therapy was completed, and he is still entirely free of any evidence of the disease process.

We have also successfully treated two patients with central nervous system cryptococcosis and one patient with disseminated sporotrichosis with knee joint involvement. Apparent cure has been obtained in the patients having a cryptococcal meningitis; however, the person with sporotrichosis has had a relapse of his joint involvement. Finally, we have had the opportunity to treat one man with pulmonary coccidioidomycosis of eight years' duration. This treatment was completed well over a year ago, and to my knowledge he is still free of any evidence of activity of his long-standing disease.

DR. LOUIS H. WINER, Beverly Hills, Calif.: Our associates, Dr. Edwin Wright and Dr. Victor Newcomer, have used amphotericin B locally, 1% in ointment in resistant moniliasis. The lesions responded very satisfactorily.

DR. GEORGE H. CURTIS, Cleveland: I should like to add to this discussion by reporting on a case of cryptococcosis. I have had a patient for some eight or nine months now, who has bone infection about the right acetabulum. This woman has had a total of 3 gm. of amphotericin B, and there appears to be some evidence of healing of the bone. It became so that we had a terrible time administering amphotericin B intravenously because of severe sclerosis of the veins. Thus, we had to administer a course by local irrigation of the bone cavity. There were no local or systemic reactions. We used 50 mg. in 100 cc. of saline per irrigation daily. The saline solution was used on the advice of Dr. Hildreth-Smith, who thought it would do very well.

I also want to call attention to the fact that, possibly, amphotericin B is not without some danger. In this particular woman, we have definite evidence that amphotericin B depressed the platelets. After repeated intravenous infusions, considerable drops in the platelet counts were observed. For example, at one time, the platelet count dropped from 200,000 to 20,000. Therefore, I believe platelet counts should be done at intervals during the courses of treatment.

DR. CARL T. NELSON, New York: I should like to mention a type of reaction to the intravenous use of amphotericin B which, I think, has not been recorded previously.

One patient of ours with systemic moniliasis was started on the relatively small dosage of 10 mg. of amphotericin B in 500 cc. of distilled water intravenously. Approximately one-half hour after the start of the slow infusion, the patient developed signs suggestive of severe anaphylactic shock: chest pain, vomiting, urinary and fecal incontinence, unobtainable blood pressure, sweating, and cyanosis. Subsequently, the temperature rose to 103 F, the BUN was elevated, and there was heavy albuminuria.

It is of interest that this patient had been given a trial of amphotericin B by mouth about six months previously. I mention this case merely to suggest that, as Dr. Curtis has just emphasized, amphotericin B intravenously may not be an entirely innocuous agent.

DR. MAURICE J. COSTELLO: We want to thank the discussers, Dr. Sternberg, Dr. Pardo-Costello, Dr. Pipkin, Dr. Harrell, Dr. Winer, Dr. Curtis, and Dr. Nelson.

We have another patient at Bellevue at the present time who is under similar treatment for this condition. It is amazing that we have gone 30 years in New York City, to my knowledge, without a single case, and two cropped up within the past year. Dr. Medd Henington sent me yesterday some slides. He expected to be here to discuss this informally.

As an example, this is a patient whom he saw with chromoblastomycosis, and he treated this patient with amphotericin B this past April (1958); that is, he treated one-half of the lesion with amphotericin B by local injection in saline. He used only 1 mg. per kilogram, whereas we used 5 mg. He gave three injections a week. He claimed there was complete resolution of the area treated, and the control area remained the same.

For illustration, here is a biopsy specimen, showing two granulomas with the epithelioid, really epithelioid granulomas. Fred Weidman brought out the fact that many of these cases may look like sarcoid, because of the epithelioid type of granuloma.

Fred Weidman also called attention to the pinkish halo around the encrusted area of the organism, which was entirely characteristic.

The problem here, of course, is not the success in the treatment of this particular case with amphotericin B, but I think that it opens up entirely new vistas in regard to the local infiltration of these antibiotic drugs in the treatment of granulomas.

Pseudohypoparathyroidism

The Seabright Bantam Syndrome

CARL W. LAYMON, M.D., and ALVIN ZELICKSON, M.D., Minneapolis

The anatomy of the parathyroid glands was described first by Sandstrom (1880). Collip (1925) prepared an active parathyroid extract which raised the blood calcium level in parathyroprivic as well as normal animals. At the beginning of this century cases were described with symptoms of hypofunction identical with those of postoperative hypoparathyroidism but with absence of the etiologic factor, the operation. This disease was called idiopathic hypoparathyroidism, and its chief symptoms are hypocalcemia, hyperphosphatemia, and decreased urinary excretions of calcium and phosphorus. The values for serum phosphatase are normal. There are symptoms of tetany and neuromuscular irritability due to hypocalcemia. These characteristic metabolic features can be corrected by parathyroid hormone, as well as dihydrotachysterol.

Pseudohypoparathyroidism is a rare disease which was discussed first by Albright, Burnett, Smith, and Parson (1942). They suggested the euphonic eponym of "Seabright bantam syndrome." This expression derives its origin from the fact that the male Seabright bantam has female feathering. The cause of the abnormality is not that the testes of the male bird produces female hormone but that the feathers of the male bird respond in an abnormal way to the normal male hormone. Another probable example of failure of an end-organ to respond normally is encountered in patients with low basal metabolic rates without other evidence of hypothyroidism. It usually requires more thyroid hormone to elevate the metabolism in these patients to normal than in true hypothyroidism. The inference is that the low basal metabolism is due to a failure of the body to react in a normal way to thyroid hormone. Still another example is the absence of the beard in the American Indian. Pseudohypoparathyroidism has the same symptomatology, chemical findings, and physical signs as hypoparathyroidism, but the cause of the disturbance is a resistance to rather than to a lack of parathyroid hormone.

Submitted for publication July 8, 1958.

From the Department of Dermatology, Minneapolis General Hospital (Dr. Carl W. Laymon, Director), and the Division of Dermatology, University of Minnesota Medical School (Dr. Francis W. Lynch, Director).

Clinical Features

Patients with pseudohypoparathyroidism present a typical physique characterized by a round face, short stature, and a stocky build. Changes in the shape of the metacarpal and, less often, the metatarsal and phalangeal bones are frequently present. The first, fourth, and fifth metacarpals and, rarely, the second, are affected chiefly, although in most instances only the first and fifth are involved. They are abnormally short and often wider than normal, and sometimes their epiphyses invaginate the diaphyses because of inequality in rates of growth.

Frame and Carter (1955) reviewed 25 cases of pseudohypoparathyroidism. Nineteen occurred in females and only six in males. The earliest age at which the diagnosis was established was 3 years and the latest 49 years. The authors stated, however, that since the preparation of their paper they had an opportunity to observe another case of pseudohypoparathvroidism,

in a baby girl aged 7 weeks. The mean age was 20 years, and an average of 14 years elapsed from the time that evidence of the disease was present to the time of correct diagnosis. Although historic data were lacking in many instances, it can be inferred that stigmas of the disease were frequently present at birth or within the first year of life.

The usual presenting symptoms of pseudohypoparathyroidism are tetany and convulsions, ranging from mild paresthesias in the extremities to muscle cramps, laryngo- and carpopedal spasm, and generalized convulsions. In one patient the major complaint was excessive drowsiness during the day without any symptoms of tetany or convulsions. In 16 of the 25 cases convulsions were described. The age of onset varied from 2 months to 18 years. In most instances there were typical grand mal attacks. In three of the patients, the convulsions were focal in nature and were confined to, or more prominent on, one side of the body. Neurologic examinations showed slight blurring of the disk margins in three cases. A positive Chvostek sign was recorded in 17 instances and a positive Trousseau in 12. Parkinsonian gait and tremor occurred in one case. The presence of mental retardation was specifically mentioned in 13 of the 25, and the average intelligence quotient was 72. In several patients there was evidence that mental retardation and slow physical development had been present since infancy. Mental retardation antedated the seizures in several cases.

Cataracts were mentioned in seven, although ophthalmologic examination was not performed in every instance.

Evidence of poor dentition, characterized by defective eruption of teeth, was present in 13.

Subcutaneous calcification is another feature of pseudohypoparathyroidism. There is no particular site of predilection. In two patients calcification was noted at birth, while in others it appeared later in life. In six, roentgenologic examination demonstrated calcification in bursas and muscles which was not detected on physical examination. About 50% of patients with pseudohypoparathyroidism have soft tissue calcification.

In most cases cutaneous lesions were not mentioned. Dryness and coarseness of the skin were present in 3 of the 25 cases which were reviewed by Frame and Carter. Evidence of superficial fungous infection of the skin, which is sometimes found in idiopathic hypoparathyroidism, was not mentioned in any of the cases. Elrick and his colleagues (1950) noted facial hypertrichosis in one of their cases and thinning of the finger nails in another. Howat and Ashurst (1957) described sparseness of hair on the scalp and face and in the axillas in one case. This patient had coarseness of the skin plus scaly lesions at the angles of the mouth. Mackler, Fouts, and Birsner (1952) mentioned that one of their patients had a florid complexion.

Laboratory Findings

Pseudohypoparathyroidism is characterized by depression of the serum calcium and elevation of the inorganic phosphorus. Frame and Carter stated that the average serum calcium level before treatment was 6.8 mg. %, with a range from 4.3 to 9.2 (normal 9-12; children 10-15). The serum inorganic phosphorus varied from 4.2 to 11.1 mg. %, with an average of 7.5 (normal 3-4.5). The findings paralleled those in idiopathic hypoparathyroidism. The alkaline-phosphatase values were either normal or slightly elevated (normal: adults 1.5-4; children 1.5-13 Bodansky units). There were no other important changes in the urine and blood. The urine Sulkowitch test was negative in those cases in which it was performed.

The round, full facies and mental dullness of patients with pseudohypoparathyroidism suggest hypothyroidism. However, in none of the cases in which tests of thyroid function were obtained was there convincing

evidence of thyroid disfunction. Glucose-tolerance tests and examinations of the cerebrospinal fluid showed no significant abnormalities.

In most cases of idiopathic hypoparathyroidism, increased density of the bones occurs. Roentgenologic examination of the skeleton of the patients of Frame and Carter showed some degree of localized or generalized increased osseous density in 5 of the 25, while in 7 there was evidence of skeletal demineralization. In two patients there were areas of increased as well as decreased density. In one patient there was generalized bony decalcification. Roentgenograms of the short fingers and toes showed that there was an early closure of the epiphyses of the metacarpal and metatarsal bones. In some the latter were thick and deformed, as well as being short. Abnormalities of the long bones were noted, such as widening of the medullary cavities, spur formation of the tibia, and bowing of the fibula. Two patients showed coxa valga and one coxa vara. The cranial vault was thick and granular in 6 of the 25 cases. Roentgenologic examination of the teeth showed shortened and defective root formation. The clinical feature of calcinosis was verified roentgenologically in 18 of the 25 cases. Ossifications were observed in the basal ganglia, muscles, ligaments, tendons, bursas, and subcutaneous tissues. Cerebral calcifications occurred alone in five cases, and in a few instances there were extracerebral soft tissue calcifications.

Five patients had intravenous pyelograms. The tests were normal in four, and in the fifth there were bilateral megaloureters without evidence of caliectasis or pyelectasis. Normal renal function ruled out the possibility that the metabolic disorder was secondary to any of the usual forms of renal insufficiency.

In the 12 of the 25 patients pretreatment electroencephalograms were recorded. Only 2 of the tracings were normal, while in the remaining 10 the findings were compatible with a diagnosis of a convulsive disorder.

The Ellsworth-Howard test is important in the diagnosis of pseudohypoparathyroidism, especially in the differentiation from idiopathic hypoparathyroidism. In the test the total urinary phosphorus excretion is determined hourly for three hours before and three hours after the intravenous administration of 200 units of parathyroid hormone (Parathormone). In order to evaluate the potency of the parathyroid hormone, a control patient should be tested also. Normal persons respond to parathyroid hormone with about a threefold to fourfold phosphate diuresis. In contrast, patients with pseudohypoparathyroidism show little or no response, usually less than a twofold one. A normal or greater than normal (up to sixfold) phosphate diuresis is to be expected in patients with idiopathic hypoparathyroidism after the administration of 200 units of parathyroid hormone. Frame and Carter felt that the specificity of the Ellsworth-Howard test is questionable, since in two of their cases there was a phosphorus diuresis greater than one should expect in a patient with pseudohypoparathyroidism. Elrick, Albright, Bartter, Forbes, and Reeves (1950) also believed that the response to the intravenous injection of parathyroid hormone may not be reliable in all instances to differentiate between the pseudo and the idiopathic forms of hypoparathyroidism.

Treatment

In 18 of the 25 cases reviewed by Frame and Carter, statements regarding treatment and response were recorded. The most effective drug was dihydrotachysterol (1 to 3 cc. daily), supplemented in most cases by calcium salts and 25,000 to 100,000 units of vitamin D. All of the patients improved, as manifested by a decrease or complete disappearance of tetany and convulsions. In three there was mental improvement. In the patient of Frame and Carter the response to treatment was gratifying. She was free of seizures for six months and became more alert. There was a gain of 9 points in her

intelligence quotient, and her mental status continued to improve with treatment. In all cases the clinical improvement was accompanied by a return of the serum calcium to normal. In many, as the serum calcium returned to normal, slightly larger doses of vitamin D were successfully substituted for the more expensive dihydrotachysterol. The frequent use of the urine Sulkowitch test and occasional serum calcium determinations were used to guard against hypercalcemia. There was no improvement in the abnormal physical characteristics.

Report of a Case

A white girl, aged 2½ years, was seen first on Dec. 2, 1946, at the University of Minnesota Hospitals because of jaundice. Feeding difficulties were encountered shortly after birth, and the child apparently had abdominal pain and did not gain weight properly. At the age of 2 months she was hospitalized because of "choking spells," at which time a diagnosis of "enlarged thymus" was made and roentgenotherapy was administered. When she was 3 months of age, she was hospitalized again because of laryngitis and tracheitis which caused dyspnea. One month later she was treated at another hospital because of respiratory difficulties. Calcium salts were administered orally but no response was noted until the intramuscular injection of vitamin D. One month later the serum alkaline phosphatase was 18 Bodansky units per 100 ml. The patient was in a hospital during her second year of life because of jaundice, hepatomegaly, and abdominal distention. During this year she had repeated attacks of bronchitis and bronchopneumonia.

Physical examination at the time of her first admission to the University of Minnesota Hospitals showed a small jaundiced white girl who was malnourished and had small atrophic extremities. The abdomen was protuberant, and the liver and spleen were enlarged. Her skin was deeply icteric, thickened, lichenified, and excoriated. The hair on her scalp was coarse and sparse. Biliary exploration was performed, and the gallbladder was removed. A biopsy specimen of the liver showed capillary thrombi and some central degeneration of the liver cells. Following surgery, jaundice receded and the patient was discharged. During the next two months jaundice disappeared completely, but the child had extreme pruritus. Three months after the patient was discharged from the hospital she developed increased tonicity of the extremities and held her hands in a peculiar manner. A diagnosis of tetany was suspected.

She was admitted to the University of Minnesota Hospitals for the second time, in 1948, when she was approximately 3½ years of age. At this time the liver was enlarged and there were numerous cutaneous excoriations. The calcium phosphatase had risen to 35 Bodansky units per 100 ml. The serum calcium was 8.2 mg. %, and the phosphorus was 6.9 mg. %. Roentgenograms of the hands and feet showed changes which suggested cyst-like spaces in the diaphyseal portions of the bones. Thickening of the carpals and metacarpals was noted, and the first metacarpals showed an expansion of the distal portion of the shaft with constriction of the central portion. Psychometric evaluation showed that the child was retarded. A diagnosis of hypothyroidism was considered, and desiccated thyroid was administered for three months. During this time the skin was less dry, and the patient seemed more alert and active.

Cramping of the muscles of the hands, feet, and legs became severe enough to require another hospital admission at the time the child was 4 years

Fig. 1. — Abnormally short digits.

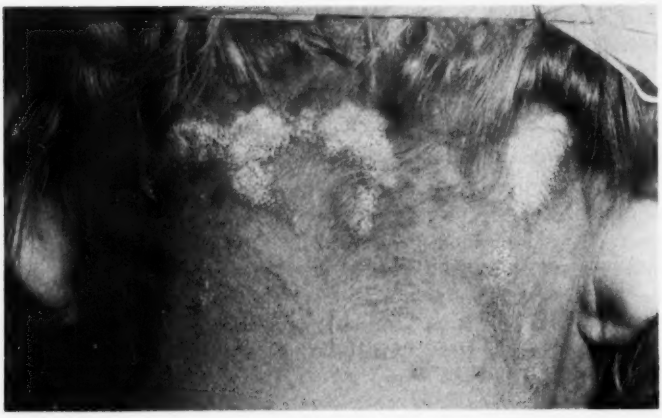


Fig. 2A.—Psoriasiform plaques in suboccipital region.

7 months of age. On this occasion a positive Chvostek sign was elicited. The serum calcium was 5.5 mg. %, and the phosphorus was 7.0 mg. %. The intravenous injection of calcium salts relieved the acute symptoms of tetany, but the oral administration neither decreased the frequency or severity of the attacks nor changed the abnormal calcium and phosphorus concentrations in the blood. The Ellsworth-Howard test showed that there was no increase in urinary phosphate excretion after the intravenous administration of parathyroid extract. Roentgenograms of the wrists and spine showed a coarsened trabecular pattern of the bones. There was hypercalcification in the distal radial metaphysis. Coarsening of trabeculation was also noted in the tarsal bones, tibia, and femurs, as well as the spine and pelvis. Examination of the eyes by means of a slit lamp showed punctate white sharply demarcated opacities in the deeper layers of the cortex of the lens, both anteriorly and posteriorly.

A diet which was normal in fat but low in phosphorus was prescribed plus a supplement of oral synthetic vitamin D in doses of 150,000 I. U. daily and calcium gluconate in doses of 9 gm. daily, which completely relieved the symptoms of tetany. Before vitamin D was administered the serum calcium was 5.9 mg. and the phosphorus was 6.3 mg. %. One week later the calcium had risen to 6.9 and the phosphorus had fallen to 4.4 mg. %. Twenty days after treatment the serum calcium was 10.8 mg. and the phosphorus was 3.3 mg. The alkaline phosphatase decreased from 70 units prior to therapy to 53.4 units. At this time there were normal amounts of calcium in the urine.

One month later the patient was readmitted to the hospital to repeat the studies of serum calcium and phosphorus, at which time the blood calcium was 9.8 mg. and the phosphorus 6.0 mg. %. The phosphatase was 58 units per 100 ml. At the time of the last admission, in Feb., 1957, the chemical changes in the serum were essentially unchanged. At this time the patient presented lichenified lesions on the posterior portion of the neck which simulated seborrheic dermatitis. There were similar changes on the right side of the face and on the forehead at the hair line. There were several psoriasiform plaques on the scalp. The skin of the entire body was dry and scaly, resembling ichthyosis, and there were numerous excoriations.

Histologic Features.—Microscopic examination of a dry scaly plaque on the right forearm showed moderate hyperkeratosis of the epidermis. There were scattered islands of parakeratosis and accu-

Fig. 2B.—Lesions on forehead similar to those seen in Figure 2A.

mulations of inflammatory infiltrate in the papillary portion of the cutis.

Comment

The diagnosis of pseudohypoparathyroidism is not difficult when all of the typical symptoms and signs are present. As more cases are reported, however, the variability of the clinical picture becomes evident. Most patients with pseudohypoparathyroidism are lacking in one or more of the aforementioned features. For instance, the fingers may be of normal length and there may be an absence of soft tissue ossifications. Occasionally, there may be normal phosphorus diuresis after 200 units of intravenous parathyroid hormone. The differential diagnosis of pseudohypoparathyroidism includes a large number of disorders. Rickets, renal insufficiency, and steatorrhea can all produce a lowered serum calcium. A past history of thyroid surgery might suggest the possibility of operative damage to the parathyroid glands as the cause of hypocalcemia.

Idiopathic hypoparathyroidism presents probably the most difficult and important differential diagnostic problem. Here the symptomatology and chemical derangements are similar to those of pseudohypoparathyroidism. Even many of the physical findings, such as cataracts, poor dentition, and mental and physical retardation are present in both entities. However, in pseudohypoparathyroidism the characteristic facies and stature, when associated with abnormally shortened digits and soft tissue ossifications, are distinctive. Moreover, in most cases there is a clear-cut difference in the response to the Ellsworth-Howard test. The final proof of the presence of pseudohypoparathyroidism would, of course, be the demonstration of normal parathyroid tissue by biopsy.

The differential diagnosis includes other causes of tetany and convulsive disorders, such as hyperventilation, alkali ingestion, and that from excessive loss of gastric contents through vomiting. Most of these conditions can be readily explained. Pseudohypoparathyroidism must be considered in patients who have been diagnosed as having idiopathic epilepsy. This is especially true if these patients are refractory to the usual anticonvulsant medications.

Pseudohypoparathyroidism should be considered in patients with dwarfism, especially achondroplasia and mental retardation. In some cases the obesity, round face, and mental sluggishness might suggest hypoparathyroidism. Myositis ossificans, in which there are shortened digits of soft tissue calcifications, may at times be confused with pseudohypoparathyroidism. In the former, however, the serum calcium is normal.

The skin is not especially helpful in diagnosis, since there are no constant nor pathognomonic lesions.

The cause of pseudohypoparathyroidism is unknown, although Albright's original explanation of the pathogenesis still seems to fit the known facts of the disorder. There is apparently no lack of parathyroid hormone. Microscopic examinations of the parathyroid have been reported in at least four cases, and the tissues were found to be either normal or hyperplastic. This suggests, but does not prove, the secretion of a normal amount of parathyroid hormone. The failure of patients with pseudohypoparathyroidism to exhibit a normal phosphorus diuresis after 200 units of intravenous parathyroid hormone suggests inability of the kidney tubules to respond fully to the parathyroid hormone. In other words, there appears to be a failure of end-organ response rather than a lack of hormone. The work of Stewart and Bowen (1952) suggests, however, that the activity of parathyroid extract is not entirely contingent on kidney function. They thought that it was possible that parathyroid hormone may have two sites of action, one the bone and the other the kidney tubules.

In 11 of the 25 cases reviewed by Frame and Carter, there was evidence that other members of the family exhibited some

traits present in the patients with pseudohypoparathyroidism. Of 14 close relatives having suggestive traits, 11 were females, emphasizing the apparent feminine predominance. The presence of short stature was noted in the mothers of four patients and in the father of one patient. One mother exhibited short metacarpals and bowing of the radius. Two of the patients were twin sisters. Another patient had a twin sister with tetany, as well as calcium deposits in the basal ganglia. From the evidence presented it appears that the genetic relationship is closer in the pseudo than in the idiopathic form of hypoparathyroidism. It may be, as suggested by Bishop and De Mowbray (1951), that any one of the major components of pseudohypoparathyroidism may be inherited independently of the others. It would seem reasonable to conclude, on the basis of present evidence, that pseudohypoparathyroidism is hereditary rather than acquired.

Our case was previously discussed by Lowe and his associates (1950). They thought that the sequence of events in the pathogenesis of the patient's disorder was as follows: Her primary disease was steatorrhea. This had been present since very early in life, though no cause for it could be determined. The steatorrhea caused malabsorption of the fat-soluble vitamins. Lowe et al. found that the absorption of vitamin A was low and that the absorption of vitamin K was poor, as evidenced by the development of hypoprothrombinemia. They reasoned that the absorption of vitamin D was poor, both by analogy with other patients in whom this has been demonstrated and by the fact that the patient responded to parenteral medication with this vitamin. Secondary to the malabsorption of vitamin D, the patient failed to absorb calcium from her intestines, which in turn caused hypocalcemia and tetany. These authors thought that all of the patients' abnormalities were due to steatorrhea. They thought that, because of continued overstimulation, the kidneys had become refractive to parathyroid hormone. They reasoned that the presence of poor absorption of vitamin D, concomitant malabsorption of calcium from a diet low in that element, and secondary hypocalcemia caused prolonged parathyroid stimulation. They mentioned that patients and experimental animals frequently become refractory to prolonged administration of parathyroid extract and that animals maintained on low-calcium diets rapidly become resistant to parathyroid extract.

The terminology in this disorder deserves brief comment. Albright, Forbes, and Henneman (1952) reported a case of pseudohypoparathyroidism in which all of the usual anatomic stigmata were present but the serum calcium and phosphorus levels were normal and the patient exhibited no clinical evidence of hypoparathyroidism. They called this new syndrome "pseudopseudohypoparathyroidism." In view of the absence of clinical and laboratory signs of hypoparathyroidism, one would expect a normal response to the Ellsworth-Howard test (phosphorus diuresis following intravenous parathyroid hormone injection). However, their patient did not respond normally to this test. Miles and Elrick (1955) reported a second case and thought that perhaps this could be explained because an impotent extract was used. Roche (1955) reported another case which was similar in some respects to that of Albright and his colleagues. It seems to us that the nomenclature of diseases is already too complicated and that the term of pseudopseudohypoparathyroidism is a good example of adding confusion to terminology. The case of Roche presented only short stature, round face, and shortening of the second, third, and fourth metacarpals, and the roentgenograms revealed exostoses with secondary metaphyseal dysplasia in both femoral necks, lower femoral metaphyses, and upper tibial metaphyses, radii, and ulnae. The term pseudopseudohypoparathyroidism probably should be discarded and replaced

in each case by a descriptive denomination, such as dyschondroplasia or exostoses with metaphyseal dysplasia or congenital skeletal malformations.

Summary

Pseudohypoparathyroidism is a rare disease characterized by tetany and convulsions, low serum calcium with elevation of serum phosphorus, symmetrical obesity with round full facies, stubby fingers, acalcification of dental roots, and mental retardation in some cases. There is a failure of the appearance of phosphorus diuresis after the intravenous administration of parathyroid extract.

It seems likely that there is an end-organ (kidney) failure to respond to parathyroid hormone, which results in the chemical aberrations in the blood present in this disorder.

Cutaneous lesions are of little value in diagnosis. In most cases the skin was not mentioned. In some cases there was cutaneous dryness and coarseness, facial hypertrichosis, thinning of the fingernails, sparseness of hair on the scalp, face, and axillas, and scaly lesions at the angles of the mouth. Flushing of the face was mentioned in one case. Our patient presented lichenified plaques on the face and neck simulating seborrheic dermatitis and lesions on the scalp which resembled psoriasis. The entire skin of our patient was dry and scaly, resembling ichthyosis.

Although the cause of pseudohypoparathyroidism is unknown, it seems to be hereditary rather than acquired. Steatorrhea may play a role in some cases.

345 Medical Arts Building (*2*).

REFERENCES

1. Albright, F.; Burnett, C. H.; Smith, P. H., and Parson, W.: Pseudohypoparathyroidism: An Example of "Seabright Bantam Syndrome"; Report of 3 Cases, Endocrinology 30:922 (June) 1942.

2. Albright, F.; Forbes, A. P., and Henneman, P. H.: Pseudo-Pseudohypoparathyroidism, Tr. A. Am. Physicians 65:337, 1952.

3. Bishop, P. M. F., and De Mowbray, R. R.: Pseudohypoparathyroidism, Proc. Roy. Soc. Med. 44:952 (Nov.) 1951.

4. Collip, J. B.: The Extraction of the Parathyroid Hormone: Which Will Prevent or Control Parathyroid Tetany and Which Regulates the Level of Blood Calcium, J. Biol. Chem. 63:395 (March) 1925.

5. Elrick, H.; Albright, F.; Bartter, F. C.; Forbes, A. P., and Reeves, J. D.: Further Studies on Pseudohypoparathyroidism: Report of 4 New Cases, Acta endocrinol. 5:199, 1950.

6. Frame, B., and Carter, S.: Pseudohypoparathyroidism: Clinical Picture and Relation to Convulsive Seizures, Neurology 5:297 (May) 1955.

7. Howat, T. W., and Ashurst, G. M.: Pseudohypoparathyroidism, J. Bone & Joint Surg. 39: 39 (Feb.) 1957.

8. Lowe, C. U.; Ellinger, A. J.; Wright, W. S., and Stauffer, H. M.: Pseudohypoparathyroidism (the Seabright Bantam Syndrome), J. Pediat. 36:1 (Jan.) 1950.

9. Mackler, H.; Fouts, J. R., and Birsner, J. W.: Familial Pseudohypoparathyroidism, California Med. 77:332 (Nov.) 1952.

10. Miles, J., and Elrick, H.: Pseudo-Pseudohypoparathyroidism: Report of a New Case, J. Clin. Endocrinol. 15:576 (May) 1955.

11. Roche, M.: A Case of Pseudo-Pseudohypoparathyroidism, J. Clin. Endocrinol. 15:964 (Aug.) 1955.

12. Sandstrom, I.: Om en ny körtel hos menniskan och åtskilliga däggdjur, Upsala läkaref. förh. 15:441, 1880.

13. Stewart, G. S., and Bowen, H. F.: The Urinary Phosphate Excretion Factor of Parathyroid Gland Extracts: A Hormone or an Artefact? Endocrinology 51:80 (Aug.) 1952.

Erythema Elevatum Diutinum

Report of a Case

WARREN L. MACAULAY, M.D., Fargo, N. D.

Erythema elevatum diutinum is indeed a rare disease. Clinicians of wide experience may deny any acquaintance with the disorder, while standard textbooks of dermatology usually dispense with the subject in a short paragraph of small print. During the past 25 years case reports or dissertations on erythema elevatum diutinum appearing in the world's medical literature have averaged less than one a year.[1,2] Erythema elevatum diutinum's entity claim has been repeatedly challenged. Its place in classification remains unsettled, and differences of opinion exist regarding its pathogenesis and histopathologic interpretation. These issues are acknowledged but purposely avoided, the sole intent being to record an example of this unusual condition.

Report of Case

A 54-year-old white farmer-mechanic was first seen on May 7, 1955. The lesions of which he complained had first appeared on the left dorsal hand and on the left elbow area six years previously. Subsequently, lesions had appeared elsewhere on the body. The advent of each new lesion was heralded by intense localized pruritus of several days' duration, after which a small papule appeared and gradually enlarged. Some lesions remained papular. Others became plateau-like nummular lesions, while still others became annular, a few circinate, and a few keloid-like. No breakdown or ulceration was ever observed. Over the years a few lesions had regressed spontaneously, leaving, in most instances, no scar or residual. However, in a few instances slight pigmentation remained at the site. The patient observed that a lesion never recurred in the same spot once it had regressed. Symptoms of "smarting and burning" were induced in the hand lesions by the irritation of a day's work, and similar symptoms developed in the anterior thigh lesions after lifting hay bales. The hand lesions were "tender" to trauma. Exposure to cold weather likewise provoked symptoms of "smarting and burning." Otherwise the patient was without subjective complaints of any kind.

A review of the patient's past history revealed that he was born in Minnesota of Scandinavian stock. He had pneumonia at the age of 6 years and mumps with orchitis at age 19. "Inflammatory rheumatism" was diagnosed at age 23, and he was confined to bed for 11 weeks at that time. Ever since, exposure to cold produced "rheumatism," characterized by stiffness in the ankles and shoulders without redness, heat, or swelling.

He knew of no relative, near or distant, similarly afflicted with this skin disorder. He denied taking any medications.

Physical examination revealed the patient to be of normal body build and weight. The right testis was atrophic. No heart murmurs were heard. All joints were freely movable and grossly normal. The blood pressure 110/70.

A total of 114 lesions was present on the skin. They were distributed chiefly over the buttocks and posterior iliac crests, the knees and anterior thighs, the Achilles tendons, the dorsal feet, the elbows and extensor forearms, and the dorsal hands and wrists. The lesions were chocolate-colored—a mixture of purple, red, and brown. Many of the le-

Figure 1

Received for publication Nov. 29, 1957.

Figure 2

sions were obtuse papules. Others were elevated nummular plaques, while still others were annular, with depressed clear centers. On the dorsal hands and elbows the lesions were rough and dry, with a light scale. Otherwise, all lesions were smooth and waxy and of a rubbery consistency. On the anterior thighs a keloid-like character was affected (Figs. 1, 2 and 3).

The laboratory findings were as follows: hemoglobin 13.4 gm.; RBC 3,980,000; WBC 6,500, with 44% lymphocytes, 52% segmented cells, 2% band forms, and 2% eosinophils. Total serum proteins were 8.10 gm. %, with 5.92 gm. % albumin. The albumin-globulin ratio was 2.85:1. The serologic test for syphilis was negative. The sedimentation rate was 20 mm. per hour (Westergren). The blood uric acid was 2.44 mg. %. A urinalysis was normal. A roentgenogram of the chest was normal. Roentgenograms of the hands and feet were normal except for a solitary small cystic lesion in the right carpal captate bone. (This finding is a common minor degenerative change and is regarded as of no clinical significance.) The ppd in the first strength was negative.

Two biopsies were performed. Specimen A was a maculopapular lesion from the right flank, and specimen B was a keloid-like lesion from the left flank. The specimens were submitted to Dr. Hermann Pinkus, of Monroe, Mich., who reported as follows:

"In Specimen A the epidermis is moderately acanthotic and hyperkeratotic without parakeratosis. The corium contains a heavy cellular infiltrate which occupies the upper half of the pars reticularis, but does not affect the papillae and the deeper portion of the pars reticularis. The infiltrate is fairly diffuse with a predilection for perivascular arrangement. It consists predominantly of neutrophilic polymorphonuclear leukocytes, many of which are pynotic and degenerating. Eosinophils are absent. Mast cells are increased in number. There are focal accumulations of macrophages containing hemosiderin. The number of fixed tissue cells of fibrocytic type is increased. The collagen shows a tendency to trabeculation, particularly around the blood vessels, with leukocytes in the spaces of the mesh work. The superficial elastic fibers of the papillae are normal; the amount of deeper elastic tissue seems decreased. The decrease probably is relative rather than absolute and is due to the presence of cellular in-

Figure 3

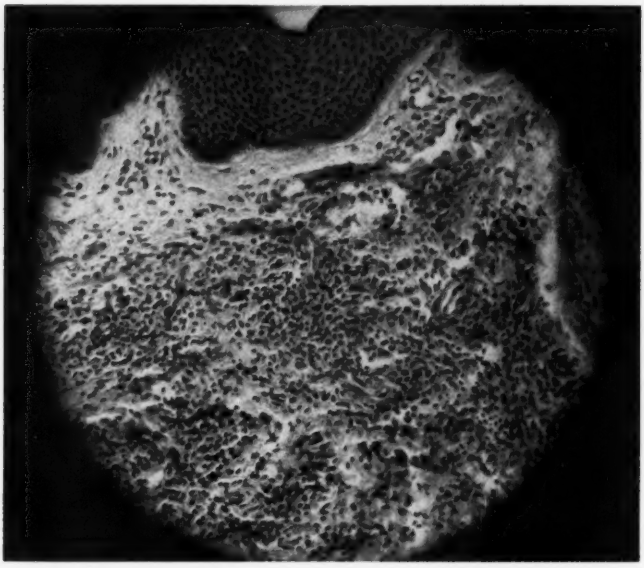


Figure 4

filtrate and new formation of collagen rather than to destruction of preformed elastic fibers [Fig. 4].

"In Specimen B the basic histologic changes are similar. There is a pronounced increase of fibrocytes and collagen. Elastic tissue is almost absent. The depth of the pathologic zone is almost double that of the first specimen. This seems to be due to new formation of fibrous tissue rather than involvement of the deeper parts of the corium. Sections stained with a modified Van Gieson procedure show moderate quantities of a yellow material resembling Weidman's 'toxic hyaline' between the red trabeculae of perivascular collagen.

"Conclusions: The findings strongly suggest a diagnosis of erythema elevatum diutinum (Weidman type), almost the only dermatosis combining a very chronic course with predominantly polymorphonuclear infiltrate. This diagnosis is supported by the presence of small amounts of 'toxic hyalin' in the perivascular tissue.

"The histologic changes do not resemble those found in granuloma annulare (Bury type of erythema elevatum diutinum). While there is some resemblance to the histologic picture of granuloma faciale, the complete absence of eosinophils and the relative lack of granulomatous features in the infiltrate seems to set this case apart from the facial granulomata with eosinophilia."

A dose of 300 r given at 110 kv., 4 ma., 8 in. distance, with 2 mm. aluminum filtration was directed at two lesions of the left ulnar forearm. This therapy appeared to have no effect whatever.

On June 8, 1955, prednisone* therapy was initiated in a dosage of 5 mg. every 6 hours for 3 days, then 5 mg. every 8 hours for 10 days, and then 5 mg. every 12 hours for 24 days, for a total medication time of 37 days. Therapy was stopped on July 15, 1955, at which time the patient reported that the lesions "felt better." Further questioning disclosed that subjectively the lesions felt "less thick" and there was "less smarting and burning" in the hand lesions. It appeared that possibly some of the lesions had lost a little of their infiltration, while a few papulonodular lesions had melted down to pigmented macular areas. However, the effects were not pronounced. Because of the patient's enthusiasm, prednisone therapy was resumed on July 27, 1955, this time proceeding with a similar dosage schedule as recorded above but continuing for a total of 50 days. A third biopsy, done on the 21st day of this second course of therapy, showed changes identical with Specimens A and B recorded above. On completion of this course of prednisone it was apparent that some involution was taking place. A few of the lesions were slowly melting down to skin level, losing their red-brown color and leaving dark brown macular pigmentation. The therapeutic effects were far from convincing, but on the patient's insistence that another course might turn the trick, prednisone was resumed on Sept. 14, 1955, in higher dosage. This time 5 mg. was given every six hours for 10 days, followed by 5 mg. every eight hours for 12 days thereafter. By Oct. 5, 1955, it was apparent

* Meticorten, supplied by Schering Corporation.

to all that prednisone in the dosages employed would not materially influence the eruption. Accordingly, prednisone was withdrawn by gradual decrements and stopped on Oct. 13, 1955. While on prednisone, the patient was fortified with potassium chloride by mouth. His weight and blood pressure remained normal during this time. No new lesions developed while the patient was on prednisone therapy.

On Oct. 19, 1955, a course of tetracycline† was instituted. Two hundred fifty milligrams was taken by mouth every eight hours for three days, after which time a mild diarrhea developed. The dosage was reduced to 250 mg. every 12 hours, and the patient continued on this medication for a total of 25 days. At the end of this time there was no apparent change in the lesions and no subjective beneficial effects were reported.

With the onset of cold weather, the patient reported on Nov. 16, 1955, that the lesions on his hands again became "sore" when exposed to the elements.

† Achromycin, supplied by Lederle Laboratories Division, American Cyanamid Company.

Summary

A case of erythema elevatum diutinum is reported. The results of therapy were unsatisfactory. Steroid (prednisone) therapy produced only slight improvement, while broad-spectrum antibiotic (tetracycline) therapy had no effect.

Fargo Clinic, 807 Broadway.

REFERENCES

1. Quarterly Cumulative Index Medicus, Chicago, American Medical Association, 1928, Vol. 3, p. 51; 1954, Vol. 56, p. 1705.

2. Current List of Medical Literature, Armed Forces Medical Library, 1955, Vol. 27, p. 1; 1956, Vol. 30, p. 664.

Laboratory Studies in a Series of Biologic False-Positive Reactors

J. LOWRY MILLER, M.D.; MARVIN BRODEY, M.D., and JUSTINA H. HILL, D.Sc., New York

The existence of the biologic false-positive reaction in the standard tests for syphilis has long been suspected. Its exact significance is as yet unknown. This report concerns a group of patients who, in the main, had no medical sign or symptom except a biologic false-positive reaction. To shed light on the significance of this finding, a variety of laboratory tests were done on each patient. These included serum electrophoretic patterns * and/or protein partitions by the Howe method; cephalin flocculation; thymol turbidity determinations; sedimentation rates; heterophil, Brucella, cold agglutinin, and cryoglobulin determinations; L. E. preparations; Coombs tests; complete blood cell counts, and urinalyses.

The importance of the biologic false-positive reaction is evident from our experience [1,2] and that of others.[3-6] From our first report,[1] in a group of 73 patients admitted to the hospital for various diseases and found to have a biologic false-positive reaction, 15.0% had acute disseminated lupus erythematosus with positive L. E. cells. From our second report,[2] in a group of 245 patients with a known persistent biologic false-positive reaction, 23.2% had a systemic disease. Of this group with systemic disease, 10.5%, all women, had systemic lupus erythematosus with positive L. E. cells. The percentage of systemic lupus erythematosus for the entire group of 245 patients was 2.4%. In an additional group of 310 patients who had only recently been observed and in whom transiency of the biologic false-positive reactions could not be ruled out, the percentage of systemic disease and systemic lupus erythematosus was essentially the same. Moore and Lutz [5] found an incidence of 6.7% of proved systemic lupus erythematosus and 4.8% of rheumatoid arthritis in a group of 148 patients with biologic false-positive reaction.

The frequency of the biologic false-positive reaction in patients with positive standard tests for syphilis has been estimated to be about 40% by Moore [5] in white patients in the upper educational and socioeconomic levels. In a recent study [7] of our material gathered largely from a clinic population, the proportion of biologic false-positive reactors was approximately 30%. This tends to substantiate the higher percentage of this reaction found in the higher economic levels. With the decline in cases of early syphilis it is to be anticipated that there will be a relative increase in the number of biologic false-positive reactors discovered by routine testing with the standard tests for syphilis.

The criteria for the diagnosis of biologic false-positive reactors must include confirmation by negative results with a specific test, either the treponemal immobilization test or one of the newer treponemal tests.

Submitted for publication July 29, 1958.

Read before the 78th Annual Meeting of the American Dermatological Association, Inc., Sun Valley, Idaho, June 6, 1958.

From the Department of Dermatology, Columbia University College of Physicians and Surgeons, Presbyterian Hospital, and the Vanderbilt Clinic.

The electrophoretic pattern determinations were performed under the supervision of Dr. Elliot F. Osserman, who interpreted the significance of these determinations as expressed in this paper.

Supported in part by the Alfred P. Sloan Foundation, the Robert Sterling Clark Foundation, the United States Public Health Service, and the National Institutes of Health Grant No. E-769 (R).

* Durrum type, Spinco Model R, Beckman Instruments, Palo Alto, Calif.

such as the Treponema pallidum complement-fixation test. In addition, there should be no history or physical findings of syphilis and preferably a negative spinal fluid examination and a reasonable lack of opportunity for exposure to syphilis.

As previously stated, this study was designed to gather laboratory information on a group of patients who, in the main, appeared well except for the finding of a biologic false-positive reaction. The majority were from our clinic in the Vanderbilt Clinic, and the remainder had been seen in private practice. All of the laboratory tests were done in the appropriate laboratories at the Columbia-Presbyterian Medical Center. The specimens for all the tests, including treponemal immobilization and standard tests for syphilis, were collected at the same time in the Vanderbilt Clinic. A few patients have been included in whom the majority of the tests had been performed in the course of a hospital admission to this institution. They have not been included in our previous published results and occur largely in the group listed with some type of systemic disease.

In the Table are listed the results of a variety of tests done on a group of 79 patients who had a biologic false-positive reaction. In the majority of instances the tests were done on each patient at the same time. The variation of the number of each test done from the total number of patients results from breakage of specimen tubes, unsatisfactory results, or failure of patients to follow through with some tests. The patients are divided into two groups. The first group, listed as nonsystemic, contains all those who had no signs or symptoms except a biologic false-positive reaction. Twelve patients are classified as having systemic disease. In this group there was one patient with each of the following diagnoses: rheumatoid arthritis, Laennec's cirrhosis, congenital hemolytic anemia, cryoglobulinemia, cerebral vascular accident, systemic lupus erythematosus, and diabetes mellitus. The eighth patient was a woman, aged 40, who, at the time these tests were made, was tentatively diagnosed as multiple sclerosis. She died six months later in another hospital of a brain tumor. The ninth patient is a woman aged 41, who has had migratory polyarthritis, transient recurring facial rash, a sedimentation rate of 70, and as yet a negative L. E. preparation. The 10th patient is a woman aged 23, who had rheumatic fever at the age of 12. She has been known to have a biologic false-positive reaction for a year and one-half and while under study developed migratory polyarth-

Summary of Laboratory Findings in a Series of Seventy-Nine Patients with Biologic False-Positive Reactions

	Nonsystemic *			Systemic		
	Normal Results	Abnormal Results	Total No. Tests Done	Normal Results	Abnormal Results	Total No. Tests Done
Complete blood cell count	59	5	64	8	4	12
Cephalin flocculation	44	23	67	2	8	10
Thymol turbidity	43	24	67	1	9	10
Sedimentation rate	51	16	67	4	7	11
Cholesterol	41	18	59	7	1	8
Urinalysis	62	4	66	11	1	12
Cryoglobulin	54	3	57	4	2	6
Protein partition	18	2	20	6	3	9
Electrophoretic pattern	21	21	42	2	2	4
Coombs test	63	0	63	7	0	7
Heterophil agglutination	55	0	55	5	0	5
Cold agglutination	56	0	56	4	1	5
Brucella agglutination	59	0	59	6	0	6
L. E. preparation	56	1 †	57	8	1	9

* Patients with no sign or symptom of systemic disease.
† Suspicious.

ritis, increased sedimentation rate, positive cephalin flocculation, and a marked increase in γ-globulin. The 11th patient is a woman aged 48, who was treated in 1936 with bismuth and arsenic for a positive standard test for syphilis, with no other evidence of this disease. In 1950 she developed grand mal seizures. A neurological work-up in 1954 was essentially negative except for the convulsive disorder. All of the tests were negative except for a positive cephalin flocculation and thymol turbidity. The 12th and last patient is a woman aged 25, who has had a positive standard test for syphilis for four years. She has an increased α_1- and α_2- and γ-globulin. The albumin was 3.1%; the globulin was 5.6 gm. %, and the sedimentation rate was 118. She is as yet undiagnosed but has generalized lymphadenopathy suggestive of a lymphoma.

The known duration of the positive standard tests for syphilis in the group with no systemic disease varies from 1 to 40 years, with a median of 5 years. For the group listed as systemic disease the median was three years for the duration of positivity of the standard tests.

The age of the men with no systemic disease varied from 23 to 76 years, with a median of 46. The age of the women in the same group was from 23 to 82 years, with a median of 44. One man, aged 59, was listed as having systemic disease. The age of the women listed with systemic disease was from 18 to 61 years, with a median of 41.

The preponderance of women over men, amounting to 71%,[2] in our previously reported series was again present here in a ratio of 15 men to 52 women in the group with no systemic disease. With systemic disease the ratio of men to women was 1 to 11.

Comment

Examination of the Table confirms the impression that the biologic false-positive reaction is an evidence, often the first, of an abnormal factor or factors associated with γ-globulin. The Coombs test and heterophil and Brucella agglutinations were consistently negative. The cold agglutinations were all negative except in the one patient with cryoglobulinemia. The L. E. preparations were all negative except in the patient with systemic lupus erythematosus and one suspicious test in a Chinese man in whom all other tests, signs, and symptoms were negative.

As seen in the Table, the incidence of normal to abnormal findings in the electrophoretic pattern determinations was one to one in both the nonsystemic and systemic groups. This abnormality of 50% was the highest found with any of the tests. A wide variation in the type of derangement in the serum protein was apparent in the specimens exhibiting abnormalities from both groups of patients. These derangements consisted of an increase in the γ-globulin fraction in 15 specimens and an increase in the α_2- and β-fractions in 7 specimens. The hypergammaglobulinemia is similar to that seen in a large proportion of patients with cirrhosis, the collagen disorders (including systemic lupus erythematosus and periarteritis), and sarcoidosis in that a diffuse increase in the γ-globulin peak is exhibited. The increase in α-globulins is considered to be a nonspecific abnormality, which is encountered with great regularity in almost all chronic disease states, including those of infectious, degenerative, and neoplastic origin.

It is notable that three patients with no systemic disease were found to have a significant decrease in γ-globulin below the limit of normal variation. In these three patients there were no other electrophoretic abnormalities. This observation of a hypogammaglobulinemia in conjunction with the observation of several other patients with γ-globulin within normal electrophoretic limits could again indicate that the positive standard test for syphilis is, in part at least, dependent upon the presence of an abnormal circulating γ-globulin and that a qualitative abnormality may be present without an electrophoretically demonstrable

increase in this fraction. It must be stressed that, although the γ-globulin appears to be a single component electrophoretically, this fraction is, in actuality, a complex mixture of a vast number of different protein constituents, which have in common their electrophoretic mobility. From this it is apparent that the hypergammaglobulinemia seen in two different disease states, such as systemic lupus erythematosus and sarcoidosis, although electrophoretically indistinguishable, may, in fact, be vastly different in the particular protein varieties represented. This thesis is substantiated by the rarity with which one finds biologic false-positive reactions in sarcoidosis [1] and lymphopathia venereum.

It is of considerable interest that in the patients manifesting laboratory evidence of a serum protein derangement in the form of a positive flocculation reaction with cephalin cholesterol or thymol, some of these patients had electrophoretic patterns within normal limits and others had a hypergammaglobulinemia. It must again be concluded that qualitative abnormalities may exist with or without demonstrable quantitative globulin changes.

In the Table it will be noted that the proportion of abnormal results with the serum protein fractionation by the chemical (Howe) method is much lower than with electrophoretic separation. This apparent discrepancy is consistent with the well-documented observation [8] that, with the Howe technique, the α-globulins are left in the albumin fraction after precipitation of the globulins. Accordingly, these pathologically increased moieties (the α-glycoproteins) are erroneously included with albumin. The electrophoretic technique permits the separation of these α-globulins from albumin, therewith resulting in a more correct quantitative result than is possible with the chemical fractionation procedure.

The cephalin flocculation and the thymol turbidity tests were positive in approximately 36% of the group without systemic disease and were positive in 8 out of 10 patients with systemic disease.

The sedimentation rate was increased in 24% of those patients with no systemic disease and in 7 of the 11 patients with systemic disease. Where consistently increased with no apparent evidence of systemic disease, it serves as a further warning of possible difficulty for the patient.

The increased cholesterol findings occurred, with the exception of two patients, in those 50 years of age or over.

The following paragraph encompasses in our opinion the proper procedure with a patient with a biologic false-positive reaction. It is based on the extent of knowledge now available on this subject. The diagnosis of biologic false-positive reaction cannot be made without confirmation by results of one or more of the specific treponemal tests. When the diagnosis is thus made, it should be followed by serum electrophoretic and sedimentation rate studies, cephalin flocculation and thymol turbidity determinations, and complete blood cell counts. If these are all negative, yearly observation—especially for joint pains, unexplained bouts of fever, and general malaise—should suffice. If some of the tests listed are positive, more careful observation is indicated, with repetition of the tests from time to time. The diagnosis of biologic false-positive reaction is always of serious significance. It is commoner and of more concern in women, especially young women, because of the higher incidence of systemic lupus erythematosus in this group. Despite the serious significance of a biologic false-positive reaction, it is evident that many patients with this finding have exhibited no apparent ill effects over many years. These variations are present in many chronic diseases. Alertness to the potentialities, careful observation, and laboratory studies are at present our best means of defense. Future research may clarify the problem.

Conclusions

In 79 patients studied with a variety of laboratory tests, 57 showed abnormality in 1 or more tests.

Sixty-seven of these patients exhibited no clinical evidence of disease except a biologic false-positive reaction. Forty-seven showed abnormalities in the laboratory tests done.

Twelve patients had clinical evidence of systemic disease, with a higher proportion of positive results of laboratory tests than those without systemic disease.

The findings of the serum electrophoretic pattern showed a wide variation in the type of derangement in the serum protein.

The tests in the order named were those showing the highest incidence of abnormality: serum electrophoretic pattern, cephalin flocculation, thymol turbidity, sedimentation rate, and complete blood cell count. The performance of these tests is advocated in patients with biologic false-positive reactions.

555 Park Ave. (21).

REFERENCES

1. Miller, J. L.; Slatkin, M. H.; Brodey, M.; Wechsler, H. L., and Hill, J. H.: Studies with the Treponemal Immobilizing Test, J. A. M. A. 154: 1241, 1954.

2. Miller, J. L.; Brodey, M., and Hill, J. H.: Studies on the Significance of the Biologic False-Positive Reaction, J. A. M. A. 164:1461, 1957.

3. Moore, J. E., and Mohr, C. F.: Biologically False-Positive Serologic Tests for Syphilis: Type, Incidence, and Cause, J. A. M. A. 150:467, 1952.

4. Haserick, J. R., and Long, R.: Systemic Lupus Erythematosus Preceded by False Positive Serologic Tests for Syphilis: Presentation of 5 Cases, Ann. Int. Med. 37:559, 1952.

5. Moore, J. E., and Lutz, W. B.: The Natural History of Systemic Lupus Erythematosus: An Approach to Its Study Through Chronic Biologic False Positive Reactors, J. Chron. Dis. 1:297, 1955.

6. Ledbetter, R. K., Jr.: Biologic False Positive STS Reactions: Possible Causes, First International Symposium on Venereal Diseases and the Treponematoses, Washington, D. C., June 1, 1956.

7. Hill, J. H., and Miller, J. L.: The Significance of Various STS Patterns in Relation to TPI Findings and Clinical Diagnosis, 8th Annual Symposium on Recent Advances in the Study of Venereal Diseases, Washington, D. C., April 25, 1957.

8. Gutman, A. B.: The Plasma Proteins in Disease, Advances Protein Chem. 4:155, 1948.

ABSTRACT OF DISCUSSION

DR. NORMAN N. EPSTEIN, San Francisco: The detection of biologic false-positive (BFP) reactors has been greatly simplified by the introduction of the Treponema immobilization test (TPI) by Nelson and Mayer, in 1949, and more recently by other tests for treponemal antibodies, such as the Treponema pallidum complement-fixation test (TPCF), the Treponema pallidum agglutination test (TPA), the Treponema pallidum immune adherence test (TPIA), and the Reiter's protein complement-fixation test. These latter tests are highly specific for the detection of treponemal disease.

The absence of treponemal antibodies in the blood serum of a patient with a positive standard test for syphilis (STS) as determined by a negative test employing a treponemal antigen is sufficient for a diagnosis of a biologic false-positive reaction. This statement requires some qualification, as it is known that the treponemal tests also give false-positive and false-negative reactions. The exact percentage of such reactions is not known, but it is thought to be rather small. A recent survey of the United States Public Health Service (USPH) in which the treponemal tests, including the Reiter's protein complement-fixation test, were compared with several STS's for syphilis in a number of different laboratories, was completed in October, 1957. The final results have not been compiled as yet, but from the material which I had the opportunity of examining, it seemed that the percentage of false reactions with the treponemal tests may be considerably higher than the 1% to 2% commonly thought to occur. As we gain more experience with the treponemal tests, the true incidence of false reactions will be determined more accurately. Nevertheless, in spite of these limitations, it may be said that a patient who gives no history of syphilis, who on careful physical examination shows no signs of syphilis, whose STS is positive and whose treponemal test is negative, should be considered a BFP reactor.

Besides releasing many patients from the stigma of a diagnosis of syphilis, the fact that BFP reactors can be detected accurately has had some very significant implications. The work of J. Lowry Miller and others indicates that a patient with a chronic or persistent BFP reaction in his blood serum may have some serious systemic disease other than and more serious than syphilis. In this group, young women with disseminate lupus erythematosus are not an uncommon finding. How-

ever, a large number of other systemic diseases have been found among patients who are chronic BFP reactors.

In his paper, Dr. Miller examined a group of 79 patients who were known to be chronic BFP reactors, i. e., with a known history of such reactions for six months or longer. He subjected this group to a battery of laboratory examinations in an attempt to find a pattern of abnormalities which would throw light on the nature of the positive STS reactions in their sera. He found that the 12 patients with evidence of systemic disease showed greater degrees of abnormality in the laboratory tests than the 67 who showed no evidence of systemic disease. In this latter group, 59 of the 67 patients showed abnormalities in one or more tests. From these results, Dr. Miller concludes that the positive STS found in this group is probably associated with abnormal globulins in their sera.

The conclusions which should be drawn from Dr. Miller's work are as follows:

1. When a patient is discovered to be a persistent BFP reactor, he or she should be subjected to a thorough study for systemic disease.

2. Those patients of this group who show no evidence of systemic disease clinically but who exhibit some abnormality in their laboratory examination should be checked from time to time, as they may be candidates for some serious systemic disease.

3. Those patients who show no evidence, either clinically or from a laboratory standpoint, of systemic disease should be discharged from care.

Dr. Miller is to be congratulated on making an important and timely contribution to a subject which is of great interest and significance to all physicians.

Dr. Charles C. Dennie, Kansas City, Mo.: This excellent presentation is a classic description of that phenomenon known as serendipity. The first part of the program in this research work was to clarify the Treponema immobilization test and, thus, negate certain factors in the diagnosis of syphilis. The second part interested Dr. Miller to such a point that the tail now wags the dog. It is an investigation of these substances that produce the false-positive reaction, substances that have pointed to the fact that other diseases then may produce similar and like substances which are responsible for the serologic reaction.

How did this come about? When the Wassermann test was devised, the pulverized liver of an unborn syphilitic child was used as antigen, and so they not only had in this liver masses of Treponemata pallidum but also the cells of the liver that had been changed by the action of those organisms in situ. One had, then, an excellent antigen, which constitutes the heart of these reactions, and that antigen was practically specific for syphilis. If we had false-positive reactions, we did not recognize them. But, as the sensitivity of the antigen was increased, so, also, was the number of false-positive reactions increased.

For a long time, our sole duty was to attempt to comfort these people by telling them that their cerebrospinal fluid was negative, that their x-rays and eyeground examinations were negative, and, if they were married, that the blood and spinal fluid of all their children would be negative. Yet, this we did not believe ourselves, because we went ahead and treated these patients anyhow, many times with tragic results.

This work has opened up a new field. As Dr. Miller said, we are still working with unknown factors producing a positive result, which is against the law of physics and chemistry; so we have to go farther with electrophoretic and other methods for extracting these small molecules of globulin, but the thing that we have to do further is not only to separate these globulins but also to divide them into their component parts and reconstruct them chemically and physically as they are now. Only when we have reached that stage at which we can do this thing can we differentiate the various diseases of which they are an index.

Dr. Stephen Rothman, Chicago: Dr. Miller is to be congratulated for his splendid study. He brought into much sharper focus what Dr. Richard Weiss told us here a few years ago, in discussing the lupus erythematosus phenomenon—that nowadays if he receives a positive serological report on one of his patients, he first thinks of lupus erythematosus and not of syphilis.

As Dr. Dennie mentioned, the biologically false-positive reactions probably will be eliminated by more widespread use of serological testing with treponemal antigens. The TPI test has been far too complicated and difficult to carry out, and so it has been practiced only in a few centers in the United States. However, the new test of Magnuson, the Treponema pallidum complement-fixation test, or, in brief, the TPCF test, seems to have become generally available. The antigen will now be on the market, and it is an extremely simple technique with which to work.

This TPCF test so far seems to be absolutely specific for syphilis, or, rather, absolutely specific for spirochetoses and trypanosomiasis. There is one interesting limitation to it, namely, that even this test has its lower threshold of sensitivity. Dr. Pearson, in our department, has demonstrated that in cases where there is good reason to believe that the patient has had syphilis—for instance, in cases of aortic aneurysms—injection of a small number of dead treponemes from a highly purified Treponema suspension has a challenging provocative action on the TPI and TPCF tests. In an amazingly high percentage of cases where there was

suspicion of syphilis and the TPI or TPCF test was negative or weakly positive, Pearson obtained this challenging effect after injection of dead treponemes from negative to weakly positive or from weakly positive to strongly positive. Numerically, such changes amount to almost 40% of his material. So, if there is really serious suspicion of syphilis, and these tests with specific antigens are negative, it is worth while to carry out this challenging test to be sure about the presence or absence of syphilis.

These tests with specific antigens have indeed opened up a new era, and all the inaccuracies of the conventional test, with normal beef heart extract, cholesterinized or uncholesterinized, and with the cardiolipin antigen have been practically eliminated.

Dr. Marion B. Sulzberger, New York: First of all, I agree with those who said that Dr. Miller and his collaborators have contributed something of great value in making the meaning of the biologic false-positive, the possible causes, the substances, etc. somewhat clearer with this careful study.

I should like to add to what Dr. Rothman has said, and to report about the use of another antigen with which we have been working at New York University-Bellevue Medical Center. At first, the late Dr. Charles Rein, and now, in his laboratory, Dr. George Kostant and Miss Louise Kelcec have been investigating the use of an antigen derived from the Reiter strain of treponeme. This antigen seems to have about the same specificity in complement-fixation and other serologic tests as antigens derived from the T. pallidum. But it has the great added advantages that it will be much easier to get and much cheaper—much safer and more practical to produce because one is dealing with a nonpathogenic treponeme which can be cultured in the test tube on nonliving culture medium. One does not need to harvest the pathogenic T. pallidum from rabbits' testes, as is necessary for preparing the other specific treponemal antigens.

Dr. J. Lowry Miller, New York: I think, with regard to what Dr. Sulzberger had to say, we are in our own laboratory finding that a rather close correspondence between the results of the Reiter antigen and the TPI tests exists. The Reiter test is a very simple one, and I hope that it can be proved to be sufficiently reliable to warrant its use in all laboratories.

I think, perhaps, we might sum up the problem we were trying to present this morning in a simple case: a young woman, 26 years of age, was very attractive; she had an excellent position, and her company said she had great possibilities with them. She was also in the position of a young woman wishing to marry. The problem she presented to us was that she had a strong biologic false-positive reaction. She told me, "If I'm going to develop one of these diseases, I do not wish to marry. I can continue with my career. I will not burden myself on someone else. If I am going to live a normal life, I would like to marry. What may I do?" This is the problem, in its simplicity.

The Education of the Dermatologist in the Soviet Union

MAXIMILIAN E. OBERMAYER, M.D., Los Angeles

There has been much interest in America concerning Russian physical and technologic sciences, but little attention has been paid to Soviet medicine. Therefore, a discussion of the Soviet medical system and particularly of our field of interest seems timely.

Dermatology in the U.S.S.R. can be understood only if viewed against its background of Soviet medicine in general.

Since, in the Soviet system, every social process is directed and mobilized toward the goals of the regime as defined by the leaders, it was inevitable that the study and practice of medicine become centrally controlled and coordinated with other phases of the Soviet social system.

Initially, the chief role of the physician was visualized as an aid in keeping the labor force on the job to fulfill agricultural and industrial quotas. Stress is placed, therefore, on preventive medicine and public health. Political indoctrination became an essential part in the physician's training, as in that of all other state employees. An important aspect of this is the extraordinary emphasis on the Soviet interpretation of the teachings of Pavlov—who has become canonized in Soviet ideology along with Marx and Lenin. Political learning, i. e. philosophy, is allotted 250 hours in the medical curriculum, which is 7 more than for physiology.

The complicated departmental structure of the Ministry of Health,* which formulates health policies to parallel the aims of

Submitted for publication July 13, 1958.

From the University of Southern California School of Medicine.

Read at the 78th Annual Meeting of the American Dermatological Association, Inc., Sun Valley, Idaho, June 4, 1958.

Mark C. Fields, Ph.D., of the Russian Research Center of Harvard University gave advice on the structure of the Soviet medical system, and Daniel Wolff, Ph.B., translated the Russian articles in the bibliography and other pertinent material.

* *Ministerstvo Zdravookhranenia S. S. S. R.*, literally, Ministry of Health Protection, U. S. S. R.

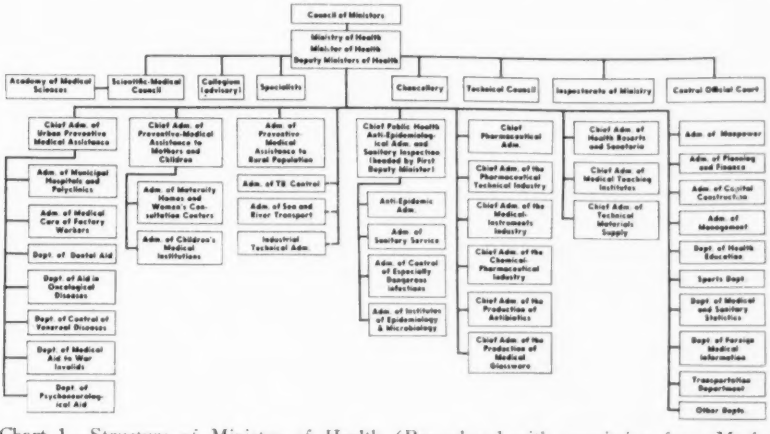

Council of Ministers
Ministry of Health
Minister of Health
Deputy Ministers of Health
Academy of Medical Sciences
Scientific Medical Council
Collegium (advisory)
Specialists
Chancellery
Technical Council
Inspectorate of Ministry
Central Official Court
Chief Adm. of Urban Preventive Medical Assistance
Adm. of Municipal Hospitals and Polyclinics
Adm. of Medical Care of Factory Workers
Dept. of Dental Aid
Dept. of Aid in Oncological Diseases
Dept. of Control of Venereal Diseases
Dept. of Medical Aid to War Invalids
Dept. of Psychoneurological Aid
Chief Adm. of Preventive-Medical Assistance to Mothers and Children
Adm. of Maternity Homes and Women's Consultation Centers
Adm. of Children's Medical Institutions
Adm. of Preventive Medical Assistance to Rural Population
Adm. of TB Control
Adm. of Sea and River Transport
Industrial Technical Adm.
Chief Public Health Anti-Epidemiological Adm. and Sanitary Inspection (headed by First Deputy Minister)
Anti-Epidemic Adm.
Adm. of Sanitary Service
Adm. of Control of Especially Dangerous Infections
Adm. of Institutes of Epidemiology & Microbiology
Chief Pharmaceutical Adm.
Chief Adm. of the Pharmaceutical Technical Industry
Chief Adm. of the Medical-Instruments Industry
Chief Adm. of the Chemical-Pharmaceutical Industry
Chief Adm. of the Production of Antibiotics
Chief Adm. of the Production of Medical Glassware
Chief Adm. of Health Resorts and Sanatoria
Chief Adm. of Medical Teaching Institutes
Chief Adm. of Technical Materials Supply
Adm. of Manpower
Adm. of Planning and Finance
Adm. of Capital Construction
Adm. of Management
Dept. of Health Education
Sports Dept.
Dept. of Medical and Sanitary Statistics
Dept. of Foreign Medical Information
Transportation Department
Other Depts.

Chart 1.—Structure of Ministry of Health (Reproduced with permission from Mark G. Field, Ph.D., and Harvard University Press).

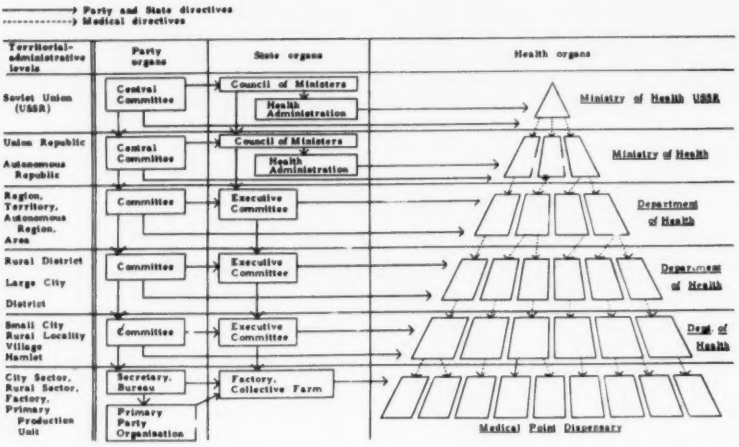


Chart 2.—Soviet medical services in relation to political (party) and governmental (soviet) authorities (Reproduced with permission from Mark G. Field, Ph.D., and Harvard University Press).

the regime, illustrates the organization of the Soviet medical system (Chart 1). The Academy of Medical Sciences advises the Ministry on medical problems and is the research arm of the Ministry, enjoying a certain measure of independence. It receives generous appropriations for many special research institutes. The Scientific Medical Council is concerned chiefly with the direction and objectives of research in line with the talents of individual scientists.

The Ministry of Health is a gigantic pyramidal bureaucracy encompassing all Soviet territories (Chart 2). The 15 republics have subordinate Ministries under which are the health units of progressively smaller areas, as regions,† districts,‡ and at the foot of the pyramid the *uchastok*,§ the basic health unit of an urban sector, a village, a rural area, etc. At each level the health unit is subject not only to supervision by the next higher unit in the health organization but also to the local political (party) and governmental (soviet) authorities.

† *Oblast*.

‡ *Raion*.

§ *Uchastok*, usually translated "district," refers to a territorial unit for dispensing medical care, not a political district.

The patient seeking medical care must apply first to his *uchastok*, which may serve a population of up to 4000 or even more. He may receive treatment there or be directed to the medical facility of a health department that embraces several *uchastoks*. If the necessary care cannot be given at this level, the patient is further directed to the larger hospitals and polyclinics of the health districts and regions. The most highly specialized medical institutes, often attached to research institutes, are in the capitals of the republics and, of course, in Moscow and Leningrad. Supplementary health units are set up at thickly populated centers: A polyclinic at a major industrial plant or a large recreational center; a local dispensary in a large dwelling unit or a small factory; "admission clinics" at large hospitals.

Undergraduate Education

Primary and Secondary Schools.—The Soviet child enters the four-year primary school at the age of 7. Methods of teaching and subjects do not differ greatly from the American pattern, except that about a third of the time is spent on mathematics and scientific studies, including biology. If progress is satisfactory, the student may be allowed to continue through the 10th

grade. Competition in schooling begins at the age of 11 or 12. In the upper grades nearly half the time is spent on science. Repeated tests eliminate the dull pupils.

After graduation, presumably between 17 and 18 years of age, the student desiring to study medicine is admitted, on competitive examination, to a medical school.

Medical Schools.—There are 76 medical teaching institutes. Independent of the universities, they are regarded more as vocational schools, being units of the Ministry of Health (Chart 1). The curriculum is a joint effort of the health and education ministries. The school year is 10 months, with a 2-month summer vacation; the medical course lasts 6 years. Both undergraduate and graduate students are supported by the State, i. e., food, lodging, tuition, and stipend, the latter being gauged on individual performance. The sixth year is devoted largely to practical experience. Most graduates must accept assigned posts regardless of location. The young physician has no title; he is simply designated as a *vrach*.‖

There are three faculties: general practice, "mother and child" or pediatrics, public health. The general practice course serves as the basic medical education to precede specialization in dermatology. Our specialty in the U. S. S. R. is designated Dermatology and Venereology, for which I shall use the abbreviation DV. As in Central Europe, the field includes gonorrhea in men (Table 1).

‖ *Vrach*, meaning physician, is not a title but, like the German *arzt*, is an occupational designation.

TABLE 1.—*Soviet Undergraduate Medical Curriculum*

		Year											
		I Sem.		II Sem.		III Sem.		IV Sem.		V Sem.		VI Sem.	
Subject	Hr.	1	2	3	4	5	6	7	8	9	10	11	12
Philosophy	250	x	x	x	x								
Foreign lang. & latin	220	x	x	x	x								
Physical cult. & train.	166	x	x	x	x								
Physics	136	x	x										
Biology	190	x	x										
Anatomy	392	x	x	x	x	x	x						
Plain & analyt. chemistry	160	x	x										
Histology & embryology	182		x	x	x	x	x						
Biologic & organic chem.	295		x	x	x								
Physiology	247		x	x	x								
Microbiology	207				x	x							
Political economy	90				x	x	x	x					
Pathologic physiology	155					x	x	x					
Pharmacology	170					x	x						
Introd. int. med. & x-ray	274					x	x						
General surgery	189					x	x						
Pathologic anatomy	184					x	x						
Operat. surg. & top. anat.	117						x	x					
Hygiene	162						x	x					
Organiz. of health presen. & history medicine	125						x	x		x			
General therapy	253							x	x				
General surg. & urology	200							x	x				
Neurology	106							x	x	x			
Obstetrics & gynecology	279							x	x	x	x		
Ear, nose, & throat	88							x					
D-V	101								x	x			
Pediatrics	166									x	x		
Psychiatry	90									x			
Medical jurisprudence	100									x	x		
Hosp. ther. & polyclinic	486									x	x	x	
Hosp. surg. & orthopedics	544									x	x	x	
Ophthalmology	80										x		
Infectious disease & epidemiology	214										x	x	

DV is taught for a whole school year, usually the last half of the fourth and first half of the fifth years. A total of 101 hours is allotted, 44 to lectures and 57 to practical sessions. The practical sessions are divided as follows: Thirty-three deal with a previously assigned topic, and twenty-six are clinical (nontopical) sessions. Subjects pertinent to our specialty seem to be fully covered.

Soviet DV Faculty Comment and Criticism of Undergraduate Program.—The problems encountered in the teaching of DV to undergraduate students in the U. S. S. R., as discussed by a number of professors of DV, are of particular interest.

Complaints of insufficiencies in the teaching program include a lack of condensed textbooks and of an atlas of dermatology and scarcity of up-to-date scientific equipment and of moulages. The number of students per class is thought to be too large. The curriculum is criticized as overcrowded with nonessential items and lacking in coordination with related subjects.

Fandeev, Yablenik, and Rakhmanov feel that 101 hours for DV are insufficient and that subjects should be redistributed.

A letter from the Ministry of Education in 1956 recommended that students be given more independence and teachers be allowed more time for investigative work. Reactions by the DV professors were controversial. Rakhmanov, among others, believes voluntary attendance should be introduced gradually and only in conjunction with higher standards for promotion. He states that voluntary attendance was regarded by students at the Second Medical Institute in Moscow as license to skip lectures, and compulsory attendance had to be restored. Khachaturian feels that profound and firm knowledge can be acquired only by painstaking independent work; independence should be stressed from the freshman year on, to avoid creation of stereotyped schoolboys. Fedorovskii suggested as a means of developing independence that practical clinics be conducted, one semester, by an assistant, with the students participating actively, and, the next, by the students themselves under adequate supervision.

Lectures.—The function of lectures in the curriculum is given much attention. Torsuev feels the entire staff of assistants and instructors should attend chairmen's lectures "in order to learn the art of lecturing and to acquire a common outlook which helps to create gradually what is called a school." Care on style as well as content is recommended, and guidance and organization are stressed as important functions. Rakhmanov believes they should include basic ideas beyond the scope of textbooks. Lecture surveys of anatomy and physiology of the skin can be omitted, according to Zenin, since they are adequately covered in texts. Rakhmanov says scientific achievement in DV, emphasizing priorities of Soviet scientists, are suitable lecture subjects; he stresses independent scientific thought and avoidance of repetition of texts. The lecturer's own opinion should be expressed, according to Torsuev, and differences from accepted opinions clarified; nevertheless, students should not be required to formulate answers at examination according to the beliefs of any particular lecturer. The custom of daily quizzes and repetition of the last lecture content is frowned upon.

As to subject matter, Torsuev says three to five lectures should be devoted to general dermatology, to history and relation of DV to other diseases, and to cutaneous physiology and morphology; this minimal foundation should precede pathology and therapy. Both Rakhmanov and Torsuev would delete lectures on psoriasis and herpes, since the student can learn about them from other sources, but feel that lectures on the following are essential: pyogenic and fungous infections, eczema, dermatitis, cutaneous tuberculosis, lupus erythematosus, neoplasms, leprosy, syphilis, and gonorrhea in men. Stressed also as desirable subjects are the working methods and progress of Soviet health agencies in DV.

Optional lectures, by *dotzenti*, assistants, and research specialists, include general and local therapy of dermatoses, physical and x-ray therapy, serologic diagnosis (Rakhmanov), and gonorrhea in men; this last is inadequately covered in the course on urology (Zheltakov).

Practical Sessions.—These are particularly singled out for reform. A warning against their deterioration into "little lectures" is sounded. The time allotted to the various subjects, and lack of a uniform program among different institutes, are criticized. According to Rakhmanov, few students are ready for practical work because of clumsy guidance and overemphasis on detail. Stress is placed on the student's adequate preparation for each topical session by study of assigned literature.

The student's practical skill is assessed at examinations conducted before the entire class. Appraisal is based not so much on oral examination as on evaluation of his work and his mastery of routine treatment and laboratory procedures. Rakhmanov feels experience in treating patients is essential to the development of clinical thinking and recommends active participation in examination of patients by students. He suggests that each student prepare, every semester, a complete report on two patients followed, the report to be considered in appraisal of his practical work. Yablenik and Khachaturian also require proof of ability to diagnose and treat the more prevalent skin diseases and syphilis and familiarity with public health aspects of skin and venereal diseases. An apparently most important feature of practical sessions deals with evaluation of temporary disability. Yablenik says the student should attend sessions of the board that passes on the degree of disability. Rakhmanov recommends that at least half the patients assigned to students be ambulatory. The importance of dispensary work is stressed by Yablenik.

A complete departure from established custom is suggested by Zheltakov: Each medical institute should have its own clinic where students, during their early years, could work as orderlies and nurses and, later, as subordinates, thus reducing the need for practical sessions.

A much-stressed feature is instruction in paper work: admission procedures, dispensary records, hospital charts, and writing of prescriptions.

Extracurricular Activities.—Students are expected to participate in study circles, pursue independent library study and research, and write essays. Extracurricular political education receives attention by Rakhmanov, who recommends that in order to inculcate the student with a feeling for socialist labor relations the teacher should set an example by his own behavior, and by Akovbian, who says the teacher should be a model socialist. Fedorovskii stresses, as valuable adjuncts to political education, "bull sessions," student study circles, and visits of faculty members to student living quarters.

DV Training in the Pediatrics Course.—Golosovker, of the Leningrad Pediatric Medical Institute, mentions the need for thorough training in DV in the pediatrics course. Writing in 1955, he stated that previously there had been no planned teaching of DV in the pediatric curriculum and that pediatricians who serve "children's collectives" were not fighting venereal diseases, fungous diseases, and pyodermias as well as they should; he criticized the absence of special dermatologic divisions in children's hospitals and clinics. He reserves half of the practical sessions in pediatrics to instruction in DV in children: 30 hours at a children's base hospital and the remainder at adult clinics. He recommends special attention to skin diseases in the newborn and infants.

Graduate Education

Medical specialization on a formal scale seems to have begun only with the fifth Five-Year Plan (1950-55): The Ministry of Health instituted a wide-scale program against venereal diseases and fungous diseases in children; the need for many more

DV specialists became apparent. Training of such specialists, however, proved much slower than expansion of treatment facilities (Studnitsin). The sixth Five-Year Plan (1956-60) envisages even farther-reaching specialized health programs, with an even greater demand for qualified specialists.

The young practitioner of medicine (*vrach*) who desires to specialize in DV may accomplish this in two ways: by a formal course in specialization as a clinical ordinator or by enrolling in an Institute for Qualification of Physicians.

Clinical Ordinator.—The preferred method is a three-year assignment as a "clinical ordinator" at a medical research institute, a higher medical institute (medical school), or a large base hospital—evidently comparable to our institutions approved for three-year residencies by our American boards.

The head of the department is held fully responsible for the work of each trainee who, after a month's work, is given an assignment individually planned for him. The first-year program is set; the second- and third-year programs are outlined but put into final form only after appraisal of progress during the first year. The trainee must report on his work to his chief every six weeks; if unsatisfactory, he is dropped.

The assignments in dermatology extend for 18 months, and in syphilis for 12 months; the last 6 months are spent in the general DV dispensary. Research is emphasized: In the words of Rakhmanov and Levin, "Education of a valuable specialist is unthinkable without arousing in him interest in research according to his state of preparedness." Additional required subjects are Pavlovian physiology, the Soviet version of biologic science, the classics of Marxism-Leninism, history of Soviet DV, and one foreign language. Specialist trainees are expected to participate in systematic ideological political work; "the inculcation of boundless patriotism and devotion to the Party" and development of critical and self-critical ¶ faculties are stressed.

Candidate of Medical Sciences.—The most talented ordinatori are retained, on the basis of competitive examination, for an additional three years' study as aspirants to the degree of Candidate of Medical Sciences. At the end of this period each aspirant # writes a thesis and defends it before a board of professors. The degree can also be achieved by working as an assistant in a research institute with an established scientist as preceptor. A successful candidate is assigned to a research institute and/or as a teacher. Before being allowed to teach, however, he must spend six months to a year at a pedagogical institute where, presumably, is learned the technique of teaching in all its phases.

Doctor of Medical Sciences.—This highest degree is achieved by independent investigative work. A special scientific commission listens to and passes on the thesis. Appointment as a professor and chairman of a DV department in a research or medical institute follows. The acme of academic career in DV is appointment to the Academy of Medical Sciences in Moscow or in the capital of one of the republics.

Institutes for Qualification of Physicians

Separate, but still somewhat overlapping the basic education in a special field, is the training provided at the Institutes for Qualification of Physicians,* of which there are 11. They are intended primarily for physicians already practicing as specialists in DV and, therefore, may be comparable with some of our university postgraduate courses and the aims of our Academy of Dermatology. The usual course lasts four months. Shorter courses are also offered by the Institutes and other facilities: a six-week assignment to a DV department of a medical school, to a research institute, or to

¶ *Samokritika*, self-criticism Soviet style—a typical U. S. S. R. institution.

Aspirantura training is the basic form of training of new academic and scientific personnel for higher educational establishments and research institutions in U. S. S. R. Literally, aspirants are "seekers" of teaching or research careers.

* *Institut Usovershenstvovania Vrachei*, literally, Institute for Perfecting Physicians.

a large hospital or DV dispensary and 10- to 30-day assignments to a DV institute for perfection in a special subject.

Central Institute for Qualification of Physicians, Moscow.—At this Institute the four-month course is apportioned as follows: skin diseases 338 hours, syphilis 156, gonorrhea 100, and antivenereal disease fight 30, making a total of 624 hours. Training is planned on an individual basis similar to that for "clinical ordinators," but subject matter necessarily is more condensed and requires maximum application on the part of the student. One subject, designated Educational Sanitation, seems to consist in the physician's lecturing to patients and answering their questions.

Leningrad Institute for Perfecting Physicians.—The recently revised four-month course at the Leningrad Institute increases the number of hours from 468 to 624. The hours devoted to skin diseases are increased from 206 to 268; to combating DV diseases, from 12 to 16; to sanitation or public health, from 60 to 110. In line with their decreasing frequency, venereal diseases are allotted less time: The hours assigned to syphilis are decreased from 116 to 64 and to gonorrhea from 76 to 66. More emphasis is placed on new problems in DV relating to physiology, endocrinology, mycology, and up-to-date therapy with antibiotics, vitamins, hormones, diathermy, isotopes, and so forth.

Problems encountered in conduct of the Institutes are discussed by a number of DV professors in the national dermatologic journal.

Rozentul, Professor of DV at the Moscow Institute for Qualification of Physicians, defines a specialist as a physician who has successfully completed the four-month course "of preliminary or primary specialization" at one of these institutes and who has had not less than three years' experience in the field. Studnitsin, however, feels the Institute course does not constitute adequate primary training in DV and holds that its function should be exclusively the raising of qualifications of specialists by periodic courses of additional training.

Tchubarova, of the Leningrad Institute, feels that instead of encumbering the course with enumeration of priorities of Soviet scientists more time should be devoted to national medicine, to ancient medicine (Chinese, Egyptian, Greek, etc.), and to critical evaluation of the French and German schools of the nineteenth century and of the present state of foreign schools, while at the same time pointing out the independence and originality of Soviet dermatology. She feels that physicians should become acquainted with the work of early Russian dermatologists, among whom she mentions P. V. Nikolsky, and should study Russian Weltanschauung, i. e., the materialistic philosophy of Lomosomov, Herzen, and others, and its influence on Russian philosophers and clinicians. The importance of the skin as an organ of immunity should be stressed. Instead of descriptive mycology, the pathogenesis, immunity, and allergy of fungous diseases should be taught. As to tuberculosis, Tchubarova says that the time could be more profitably spent in explaining the complexities of the disease than in a detailed enumeration of 11 priorities of Russian scientists in tuberculosis.

Particularly vexing in the graduate program is the choice of candidates. The comments of the professors are illuminating:

Tchubarova tabulates the 442 physicians who were sent to take courses in DV at the Leningrad Institute for Perfecting Physicians during the period 1949 to 1956. Only 18% had had previous experience or training in DV. The majority, 20%, were demobilized army physicians, while the remaining 42% were administrators, general physicians from small districts, and even specialists qualified in fields other than DV, as pathologists, surgeons, pediatricians, and sanitation and laboratory officials.

Most of the Soviet essayists condemn the practice of sending physicians without training in DV or specialists in other fields to the DV Institutes; this is considered wasteful of highly-trained manpower. The consensus is that the fault lies with the local

authorities. In rural areas, especially, because of the difficulty of replacing medical personnel, party functionaries and government authorities may be unwilling to release their local physicians who are eligible for specialist training or may assign to courses in DV physicians whose backgrounds are unsuitable. In some instances the available funds simply are not utilized. This shortsighted administration results in disadvantages to the district. For instance, eligible physicians, after being trained, could pass on to local colleagues their specialized knowledge. Also, isolation of local physicians by neglect to utilize the opportunities for training denies the community improved facilities and other health needs that could be obtained through the local physician's firsthand report to the central authorities (Rozentul).

Research Institutes

The DV Institutes for Research are of particular significance to the advance of the specialty, not only in provision of opportunity for graduate education of high degree but also in the caliber and scope of their investigative activities. There are ten such Institutes. Four are in the Russian Federative Republic (Moscow, Gorky, Sverdlovsk, Ufa), and the other six are located in the White Russian Republic (Minsk), the Ukraine (Kharkov), Uzbekistan (Tashkent), Kazakstan (Alma-Ata), Turkmenstan (Ashkhabad), and Tiflis (Georgia).

On my visit to Moscow in 1957 I visited the Central Scientific Institute for Investigation of Dermatology and Venereology. This is the principal institute for DV research in the Soviet Union; its director is N. M. Turanov. An 80-bed hospital is operated in conjunction with the institute. I was particularly interested in a number of the projects (Table 2).

In the department of R. Y. Malikin experiments are being carried out with electronic sleep induced by a current comparable to the α-waves of the electroencephalogram. Since the majority of their subjects were patients with disseminated neurodermatitis

TABLE 2.—*Central Scientific Institute for Investigation of Dermatology and Venereology of The Ministry of Health, U. S. S. R.*

Departments of Investigation			
Division	Subdivisions	Laboratories	Administrative
Dermatology	Adults Children	New drugs	Administrative & clerical facilities
Mycology	Exper. mycol.		Buildings, service, & maintenance
Leprology	Exper. diag. Clinical		
Syphilology	Adults Children Nervous sys. Inter. organs		Dept's: Scientific library, Pharmacy, Museum, Moulages, Macrofilm, Microfilm
Gonorrhea	Adult Children		
Microbiology		Microbiol. Exper. syph. Clin. diag. Serology Biopyologic	
Pathophysiology	Exper. dermat. Funct. diag.	Biochemical Radiology	
Pathomorphology Physical X-Ray therapy			

—a disease that long has held my interest—I hope to make this work on electronic sleep the subject of a separate essay (that is, after I have penetrated farther into the difficult Pavlovian concept of protective inhibition on which it is based).

The department of Experimental Syphilis is headed by N. M. Ovchinnikov and staffed by a dozen other scientists and a score of laboratory technicians. I was shown cultures of Treponema pallidum on liquid and dry media and the results of studies of the organism by the electron microscope.

Projects in Experimental Allergy are directed by P. M. Zalkan. His work is concerned chiefly with the differences in cutaneous reactivity of man and animals. He has a large number of animals, including monkeys, at his disposal.

The Department of Mycology is supervised by A. M. Arievich. Fungous diseases apparently are a greater problem in the Soviet Union than in the U. S. and are subjected to intensive study. The long introduction to Arievich's "Atlas of Fungous Diseases"—a copy of which he was kind enough to give me—bears witness to the nationwide drive to combat dermatomycoses. Their chief interests at that time were the mutability of dermatophytes, which allegedly has nullified the value of Sabouraud's classification, epilation by local application of compounds other than thallium acetate, and treatment of infections of the nails.

The Economic Aspect

Information on the economic status of the physician is contradictory. Some sources indicate a high economic position; others, a low level. It seems, however, that the medical profession is not a prestige occupation and compensation is correspondingly low. The basic salary of a general practitioner is said to be lower than that of any qualified industrial worker. A specialist, however, earns more; his salary may perhaps equal that of an engineer—an occupation definitely of the prestige class.

Science rather than the medical profession as such has preferred status. The practitioner of medicine is—correctly—not considered a scientist, but the physician with advanced degrees and employed in research and teaching gains stature and increased compensation. Many scientifically accomplished dermatologists hold at least two posts, head of a department in a research institute and a "chair" on the faculty of a medical or postgraduate institute; both positions pay full salaries. Membership in the Academy of Medical Sciences or, more rarely for a physician, the Academy of Science, also carries financial compensation, as does the writing of articles and books, or the translation of foreign scientific material. On conferment of the degree of Candidate of Medical Sciences the salary is doubled, and with the degree of Doctor of Medical Sciences it is doubled again. Thus it is more than likely the leaders in dermatology receive at least 10 times the basic salary of a general physician. It evidently pays to belong to the medical scientific hierarchy.

Indicative of the economic status of the physician is the high percentage of women, the majority of whom are among the *vrachi;* this proportion decreases sharply in the higher ranks. The relatively high number of women in the field reflects the view that men are needed for more important and more exacting tasks.

Comment

I have tried to present a picture of education in DV in the Soviet Union, interest in which was stimulated during my brief visit to Moscow in the summer of 1957. Data gathered during so short a stay, however, lacks preciseness and, since obtained with the help of interpreters, may not be entirely accurate. Attempts to clarify my impressions by letter have been unsuccessful. While information is given liberally to the visitor, it is not so readily obtained by correspondence. Much written in this country about education in Russia is contradictory, and many of the Soviet publications read in the original seem more concerned with what

should be done than with what actually is done. Nevertheless, I feel that the following impressions have a fair degree of accuracy.

Education in DV is in a fluid state with constant expansion of facilities and attempts at improvement of both undergraduate and graduate teaching. An urgent need for a greater number of qualified dermatologists is recognized by national health authorities.

The freely voiced complaints of leading dermatologists in the national dermatologic journal point to considerable freedom of expression. Evidently no holds are barred as long as Soviet ideology is held inviolate.

The problems they encounter in teaching DV to undergraduate students are both like and unlike those we face. The complaints about not enough hours, overcrowding of curricula with nonessentials, lack of coordination with related subjects, too many students in a class, their reading only abbreviated texts or abstracted lectures, their lack of independence, and their desire to be spoon-fed are only too familiar.

Their criteria for the perfect lecture, both in style and content, are of the European tradition. So also is the role of a department head: For example, the entire staff must attend the chairman's lectures to undergraduates, a stipulation we would find impracticable even in the few institutions with full-time staffs. Nevertheless, the prevailing informality of our lectures has its shortcomings; nothing will fire the imagination of a student more than an inspiring lecture.

Their problems in enforcing compulsory attendance do not exist here, since the American medical student—unlike his European counterpart—is not looked on as "a gentleman who knows what he wants and chooses accordingly." It would seem that in Russia, whose traditions of higher education were those of Central Europe, there is under way—after four decades of strict schoolboy regulations—a partial reversal toward the European liberal academic way of student life.

The instruction given seems up to date as to subject matter and probably is comparable in quality to that in the U. S. Emphasis on prevention of venereal, fungous, and pyogenic diseases rather than on medical care of the individual patient is in keeping with guided socialized medicine. The interest of the Ministry of Health in DV is likely motivated by the significance of occupational cutaneous disease in industrial output. The customary teaching of a foreign langauge (English, German) in both undergraduate and graduate systems is a requirement that has been dropped in our medical schools. To us, of course, the most alien element in the Soviet medical curriculum is the political indoctrination. Their preoccupation with the student's so-called free time—the study and research circles, work in libraries, and writing of essays—cannot be criticized.

Their practical sessions have no counterpart in our medical curricula. Since Soviet medical training does not include the rotating internship as we know it, the desire, so strongly voiced, to have the student master the practical aspects of the specialty before graduation is logical.

Neither American nor Central European is the custom of assigning to the student a patient for study and report. It is, however, a feature of medical instruction in some Latin American universities. The advantages are obvious: The student is required to follow closely the course of his patient's disease, with or in spite of treatment, and to delve into the literature. He not only learns "how to look up things" but also reveals any investigative talents he may have.

The required teaching in "paper work" makes one think of the increasing time such details require in the American doctor's office today. The emphasis on evaluation of disability is consistent with the Soviet physician's role in keeping the labor force on the job.

Graduate study appears amply provided for and subject matter well covered, but the choice and recruitment of candidates for postgraduate work present difficulties.

The research institutes, judging from that which I visited, are model facilities, liberally financed, and well provided with laboratories and animals for experiment. If the Central Institute in Moscow is the prototype, research in our field is of high degree. I was particularly impressed with the caliber of the physicians in charge; they seemed to be dedicated scientists. Undoubtedly, we should learn much from exchange of views with Soviet dermatologists, from testing their theories, and from comparing results.

3875 Wilshire Blvd. (5).

BIBLIOGRAPHY

Akovbian, A. A., and Kamzolova, K. P.: Methods of Teaching Dermato-Venereology in Medical Institutes, Vestnik dermat. i venerol. (No. 4) 31:29, 1957.

Arievich, A. M., and Stepanicheva, Z. G.: Atlas of Fungous Diseases of the Skin, Moscow: Medgiz, 1951.

DeWitt, N.: Soviet Professional Manpower, Washington, D. C.: National Science Foundation, 1955.

Fandeev, L. I.: Some Problems in the Teaching of Skin and Venereal Diseases in Medical Institutes, Vestnik dermat. i venerol. (No. 4) 31:34, 1957.

Fedorovskii, A. N.: Improvement of Practical preparation of students in dermatology and venereology faculties, Vestnik dermat. i venerol. (No. 4) 31:35, 1957.

Field, M. G.: Doctor and Patient in Soviet Russia, Cambridge, Mass., Harvard University Press, 1957.

Golosovker, S. Y.: On the Subject of Preparation of Pediatricians in the Field of Dermatology, Vestnik dermat. i venerol. (No. 6) 29:29, 1955.

Khachaturian, G. Kh.: Teaching Method and the Independent Work of Students of the Dermatological Faculty, Vestnik dermat. i venerol. (No. 4) 31:36, 1957.

Leake, C. D.: Medical Education in the U. S. S. R., J. M. Educ. 32:269, 1957.

Rakhmanov, V. A.: Problems of Teaching of Dermato-Venereology in Medical Schools, Vestnik dermat. i venerol. (No. 4) 31:25, 1957.

Rakhmanov, V. A., and Levin, A. M.: The Preparation of Clinical Ordinators in the Departments of Skin and Venereal Diseases of Medical Institutes, Vestnik dermat. i venerol. (No. 3) 27:24, 1953.

Rozentul, M. A.: The Preparation of Physician Specialists in Skin and Venereal Diseases, Vestnik dermat. i venerol. (No. 6) 27:48, 1953.

Studnitsin, A. A.: The Conditions of Dermato-Venereologic Personnel and the Immediate Problem of Its Training, Vestnik dermat. i venerol. (No. 1) 31:3, 1957.

Tchubarova, A. S.: The Program for Improving and Perfecting Physicians in Dermato-Venereology, Vestnik dermat. i venerol. (No. 2) 31:41, 1957.

Torsuev, N. A.: Lectures on Dermato-Venereology, Vestnik dermat. i venerol. (No. 4) 31:33, 1957.

United States-U. S. S. R. Medical Exchange Missions 1956, Public Health Monograph No. 50, Government Printing Office, 1957.

Yablenik, B. S.: The Teaching of Dermato-Venereology in Medical Institutes, Vestnik dermat. i venerol. (No. 4) 31:38, 1957.

Zenin, A. S.: Concerning the Problem of Teaching the Course of Dermato-Venereology in Medical Institutes, Vestnik dermat. i venerol. (No. 4) 31:31, 1957.

Zheltakov, M. M., and Studnitsin, A. A.: Reconstruction of Teaching of Dermato-Venereology in Medical Institutes, Vestnik dermat. i venerol. (No. 4) 31:30, 1957.

ABSTRACT OF DISCUSSION

DR. ADOLPH ROSTENBERG JR., Chicago: My discussion of Dr. Obermayer's paper will necessarily have to be at a theoretical level, inasmuch as I have never been to Russia and my knowledge of the subject is entirely secondhand. I shall comment briefly on three aspects of Russian medicine in general: (1) the teaching of undergraduate dermatology in the U. S. A. vs. the U. S. S. R., (2) scientific attitudes in the U. S. S. R. and the influence of the political system upon them, and (3) the impact of the socialistic system of medicine on the patient.

Dr. Obermayer has considered the undergraduate teaching of dermatology in Russia adequately, and it would be futile and repetitious for me to comment further. You have heard that 101 hours are allotted to it. In this country there is a marked variability in the number of hours allocated to the teaching of our specialty. In a sample of 13 medical schools scattered widely over the country between 16 and 101 hours were used for instruction in dermatology, with an average of 52.5 hours. The small number of hours given to dermatology in many of the schools bespeaks the meager importance with which our specialty is held by our medical colleagues. Parenthetically, it would seem that organized dermatology should initiate and support a movement to raise the prestige of dermatology among our colleagues and to give it its rightful place in the medical constellation.

Turning to Russian medicine and Russian science in general, I do not think that this audience needs to be informed that it is at a relatively high level. There is, however, one important difference between Russian science and ours in that their science is dominated by their political ideology. In school, as has been pointed out, physicians must take courses in what is known as Marxism-Leninism and must adhere rigidly to the political formulation as outlined on high. In politics this may not be too important, but when this rigid insistence upon conformity is carried over into science it can lead to nonsense. In the U. S. S. R. "truth" can be arrived at by political fiat rather than by objective verification. To give one small illustration, Budanov, in an article on "Dermatological Progress in the U. S. S. R." (*Rev. Eastern M. Sc.*, No. 2, p. 18, 1956) states that dermatology in Russia today is dominated by the teachings of Pavlov. In 1950 these teachings were declared to be unimpeachable. Now, all of us would agree that Pavlov was a great scientist and that most of his views were probably correct, but to assert that his views are unimpeachable removes them from the realm of science and transfers them to the domain of religion.

A final word concerns the attitude of the patient who has been reared in a socialistic scheme of medicine. Field, in his book, "The Doctor and Patient in Soviet Russia" (Harvard University Press, 1957) gives some interesting information. Russian emigres were interviewed in Munich and in New York. In Munich they were asked whether they preferred German or Russian medicine, and in New York, American or Russian medicine. In Munich about 50% preferred the German system and 20% the Russian; whereas in New York the figures were reversed with respect to American versus Russian systems of medicine. Now, why this striking discrepancy? Field suggests that it is because the Russian émigré prefers a socialistic scheme of medicine. This is what he is used to, and he looks at all other systems with distrust. In Germany he got this and preferred the German system because of superior equipment. In the United States, he did not get this and, even though he is willing to concede that the equipment may be superior, he still prefers the other system. Indeed, he views with misgivings physicians who are paid for their services. I think it important that we understand this, for those of us who have been reared in a private practice system find it difficult to believe that any other system could be satisfactory. Yet, was it not Ignatius Loyola who said, "Give me a boy until he is eleven, and you can have him for the rest of his life."

I should like to thank Dr. Obermayer for bringing to our attention some interesting points in the broader aspect of medicine.

DR. REES B. REES, San Francisco: I read Dr. Obermayer's paper, and feel at the moment that I know more about dermatological teaching in the U. S. S. R. than any other country with the exception of the U. S. A.

Similarities of aims in dermatological training in the U. S. A. and the U. S. S. R. are more striking than the differences, with the glaring exception of the political ideological aspects. Preoccupation with Pavlovian physiology almost amounting to a religion has its counterpart in the near deification of the various schools of thought in psychiatry in the western world, if I might name one example.

Physicians in the U. S. A. and the U. S. S. R. complete medical training at about the same age. Although the U. S. S. R. medical curriculum nominally is six years in duration, some of their subjects are taught in our premedical years, and one of those six years corresponds vaguely with our internship year. At our institution, the University of California, there are 36 hours of undergraduate dermatological teaching, but these are diversified and calculated to give maximum exposure to the subject. Venereology is separate and is now taught largely in courses in public health and urology. So few cases of early syphilis and gonorrhea are seen as to make practical experience in management difficult. Apparently, these problems remain common in the U. S. S. R.

As to the most desirable methods of teaching, one may paraphrase Samuel Johnson in saying that while one teacher is casting about for a method, another already will have the student half educated.

As to graduate training, the three-year program leading to the clinical ordinator title apparently is comparable to the present requirements of the American Board of Dermatology. The alternate U. S. S. R. method has already been abandoned here.

The higher schools of training at first make one think of Bob Hope's remark that one nowadays must have a college degree to get into high school. However, all American dermatologists who hold positions of eminence have endured comparable trials and ordeals. It is only the Civil Service aspect of this higher training that seems so formidable.

We must not now give way to Deweyism in American medical education, even though the variability and fluidity of the American system appeals most to those of us nurtured in this country. Much can be learned from interchange of ideas with dermatologists in the U. S. S. R., and we should not be influenced by the bad manners and immorality of the American lay press in pursuing our relationships with our fellow physicians.

To quote Hesketh Pierson, I have never read Karl Marx's "Das Kapital," I do not intend to

read it, and, indeed, I would rather die than read it. However, dermatologists in the U. S. A. and the U. S. S. R. belong to the same discipline, and we should take advantage of this fact. One must not lose sight of the fact that science in the U. S. S. R. includes such subjects as history but not medicine. Medicine remains more of an art than an exact science, there and here. The idea of including special training in paper work, which Dr. Obermayer did not have time to elaborate on, is not half bad. It has been shown that in this country the factor of single greatest importance in preventing malpractice actions is the keeping of good records.

I do not agree with the comment by one Russian dermatological educator that psoriasis and herpes should be deleted from routine undergraduate training. It is those very subjects for which we do not have specific treatment that give us so much difficulty in management. We should emphasize management in dealing with the complexities of these common diseases.

Finally, these two specific ideas of electronic sleep and development of topical-chemical epilators for scalp ringworm are exciting, and I should like to know more about them.

DR. MAXIMILIAN E. OBERMAYER, Los Angeles: I am glad that Dr. Rostenberg emphasized the insufficient hours allotted to dermatology in the average medical school in the United States. The school I serve has a very poor record in this respect, but so far I have been unsuccessful in improving the situation.

Dr. Rees is right about the similarities in the curriculums and the teaching methods here and in the U. S. S. R.; however, some of the dissimilarities are very significant. I enjoyed his clever remark likening the canonized Pavlov to the canonized Freud.

The preparation used for epilation is a supposedly nontoxic ketone. It is applied daily to the same spot on the scalp and, on the 10th to the 12th day, is said to bring about epilation of the entire scalp by affecting the nerve receptors.

The discussion would indicate I have succeeded in arousing interest in the subject, which is essentially what I intended.

Correspondence

EDUCATION OF THE DERMATOLOGIST IN RUSSIA

To the Editor: Soon after I had presented my paper on "The Education of the Dermatologist in the Soviet Union" at the Sun Valley meeting of the A. D. A. last June, I received a 13-page letter from Dr. N. M. Turanov, director of the Central Scientific Institute for Investigation of Dermatology and Venereology in Moscow. In this carefully detailed reply to questions I had posed in a letter to him dated Feb. 3, 1958, Dr. Turanov gave a comprehensive account of graduate education and research activities of the Institute. Since my presentation had to be completed without benefit of such pertinent and direct information as contained in Dr. Turanov's letter, I should like to ask that the following digest of his statements—so far as they bear on what was said in my paper—be made available to readers interested in the subject.

It is pointed out by Turanov that the training of the dermatovenereologist has an informal beginning in the fourth year of medical school. Students who seem particularly interested in DV are encouraged to enroll in study groups organized by the DV department to delve into the subject more deeply than is provided for in the regular curriculum and—to use Turanov's expression—interest in the specialty is grafted.

As to graduate education, in DV there is some discrepancy between my statements and those of Turanov. He says that the specialist training at the Institutes for Perfecting Physicians comprises a five-month course (780 hours) and is designed to provide DV physicians capable of working independently as house physicians in the venereal dispensaries and the DV departments of hospitals and polyclinics, and as heads of so-called "venereal points." This form of training is probably the "preliminary and primary specialization" mentioned in my discussion of these Institutes for Perfecting Physicians but covering five months rather than four, as specified in the data available to me last year. This type of training can also be obtained in the large specialized hospitals.

Of importance also in raising the qualifications of DV physicians are the DV societies in various cities, the activities of which usually are under the leadership of the DV departmental chairmen in the Medical Institutes or of the faculties of the Institutes for Perfecting Physicians and the Research Institutes. The difference between the plan of organization of these DV societies and that of our purely voluntary local and regional dermatologic societies is obvious.

One of the features of Soviet medicine, to which we have no parallel, is the consultation service provided by the Research Institutes. Through such facilities practicing physicians in all areas of the Soviet Union are provided with answers to "thousands of questions" every year.

The dispensary in the U. S. S. R. is far more complex than what we understand by that term. It is a special institution, consisting of a hospital and a polyclinic, devoted to treatment and prophylaxis. There are tuberculosis, DV, oncology, trachoma, psychoneurology, and "antigoiter" dispensaries. The work of the DV dispensaries includes not only treatment but also compulsory registration of venereal and certain cutaneous diseases, search for contacts, serologic testing of pregnant women, search for and prophylaxis of venereal and infectious cutaneous diseases in institutions for children and other medical institutions, and guidance in the fight against such diseases. The dispensaries also attempt to raise the standard of knowledge of DV in related specialties and also participate in research.

As to the work in the Central Scientific Institute for Investigation of DV, on which I commented under the heading Research Institutes, Turanov points out that the fight against the dermatomycoses is no longer a national problem and states that the mutation of dermatophytes is an established fact, also that pleomorphism has been proved to be nothing but a reversible mutation. My remarks on the department of pathophysiology (R. Y. Malikin) were directed chiefly to experiments with electronic sleep. Turanov, however, says that electronic sleep is only one of the many new modes of therapy under investigation. He says that research is concentrated on the pathogenesis of eczema, neurodermatitis, psoriasis, lupus erythematosus, scleroderma, chronic urticaria, chronic pyodermas, and bullous diseases. This

department is also devoting a great deal of attention to the nervous and humoral mechanisms in the pathogenesis of dermatoses and to research based on the works of I. A. Pavloff and on N. E. Vedensky's concepts of parabiosis and perielectrotonus, A. A. Ookhtomsky's "dominante," L. A. Orbel's ideas on the adaptive-trophic role of the sympathetic nervous system, A. D. Speransky's "nervous trophism," and K. M. Bykoff's corticovisceral and corticodermal reciprocal relations. Also under investigation are the topographic variations of cutaneous function, including the involved mechanisms, and a great number of biochemical and electrophysiologic problems. Studied also are the mechanisms in the action of ionizing radiation, of radioactive isotopes, and of new substances that shield against radiation.

What I called the Department of Experimental Syphilis is actually the Department of Microbiology, which embraces viral and serologic studies, as well as those of syphilis.

P. M. Zalkan's work, which I mentioned briefly in my comments on the Central Scientific Institute, concerns primarily the biologic-evolutionary aspects of cutaneous physiology and comparative cutaneous pathology.

Although I had hoped to receive an answer to my questions in time to verify and elaborate the information on which my paper was based, I can but be gratified that Dr. Turanov should have written to me in such detail and at such length concerning the wealth of research currently being pursued in the U. S. S. R. Unfortunately, restrictions on the space allotted to communications of this nature do not permit me to discuss here, or even to list, the investigations described by Dr. Turanov. His cooperation in providing this information certainly suggests that free exchange of scientific knowledge may not be too high a goal at which to aim.

M. E. Obermayer, M.D.
3875 Wilshire Blvd.
Los Angeles 5

On Sudden or Rapid Whitening of the Hair

ALFRED J. EPHRAIM, M.D., Brooklyn

"One of the oldest problems of pathology and physiology which has escaped scientific research and is still clouded in mythical darkness is the sudden whitening of the hair. I call it a mythical darkness, because the reports, dating mostly from older times, sound more like fairy tales than scientific observations."

These words, written 100 years ago by Landois [23] in Virchow's archives, hold just as true today. History and legend are full of stories of people who grayed suddenly after severe emotional stress. Among these storied people are Queen Marie Antoinette, said to have turned white after hearing her death sentence; Ludwig the Bavarian, after having condemned his wife to death; Ludovico Sforza, after his capture by Ludwig XII; Guarini de Verona, after noticing the loss of an irreplacable old Greek manuscript, and the Spaniards Dideo and Diego Osorio, under torture. Isabella di Guerazzi reported the case of Mr. d'Andelot, whose beard and eyebrows turned white in the areas on which his hands rested when he heard of the death sentence of his father by the Duke of Alba. These and similar stories are cited by Bodin [5] and Voigtel.[42]

Where does medical science stand on this issue today? Is it truth or fiction?

It seems physiologically difficult to understand how the hair, which, once formed, is a structure without nerves or blood supply, can throughout its length undergo rapid physicochemical changes directly due to emotional influences. But the medical literature of the last 150 years records a great number of these cases. Close scrutiny of the reports reduces the actual number of reasonably reliable cases. A few extraordinary cases are repeatedly cited by different authors and have reappeared again and again in literature. On the other hand, many patients may not have consulted physicians concerning this condition. One therefore may assume that the number of such cases is more numerous than those actually reported.

Before presenting a case recently observed by me, I shall summarize the cases reported in the medical literature since 1800. The first group comprises cases where the sudden whitening is said to have been caused by fright, excitement, or mental stress; the second group consists of reports of whitening resulting from acute organic illness.

Review of Literature

Group A (Caused by excitement, fright, or mental stress).—This group comprises 26 cases, which are reported in the literature by physicians without giving detailed medical history.

Parry [30] (1861) reports the following famous case, which has been repeated several times in literature. A staff surgeon gave an explicit account of a Sepoi of the Bengalese Army, taken prisoner, who during an examination showed intense horror and despair and turned completely gray in 30 minutes. Similar cases have been reported before by M. Cassan [8] (1827) and Bichat [3] (1834).

Pohl-Pincus [31] (1905) accounts in his book "Das Haar" for five incidents concerning four physicians and a logger who turned gray after hair-raising experiences.

From World War I only four cases have been reported: Bernard [2] (1925) (also reported by Fafner) tells of a woman spy

Submitted for publication June 27, 1958.

From the Department of Dermatology and Syphilology of the New York University Post-Graduate Medical School (Dr. Marion B. Sulzberger, Chairman).

caught by the French who turned gray overnight after being sentenced to be shot. Bernard's father attended the trial and execution as a French officer and gave a minute description. Behring,[1] Fritsch, and Vignolo-Lutati[40] (1918) report cases of soldiers who turned white shortly after terrible battle experiences.

It is surprising that I could not find any reports of graying caused by mining disasters or after the horrible experiences of World War II.

The great number of railway catastrophies of the last century account for another three reports by Schoenhoff,[37] Ellis (1861), and Schmidt.[36] One case was reported by Baelz (1908) of sudden graying of a woman after being shipwrecked.

Holzgraefe[21] (1947) cites the following two cases: 1. A 34-year-old mountain climber was in danger of his life. Several days later the hair on the right side of his head turned gray and fell out. 2. A 58-year-old woman turned gray overnight after having been told that her two sons were poisoned by gas. Her father had also turned white suddenly at the age of 46, when his house caught fire.

The following five cases are reported individually:

Ornsteen (1930) tells of a woman who received a call at 2 p. m. informing her that her child had been in a serious accident. She was snow white when her husband saw her at 5:30 p. m. Her hair had been normal when he had left her at 9 a. m. that morning, and no gray hairs had been observed before.

Macleod[26] reported that seven weeks after a motor accident a man, 46 years old, noticed white patches on his hands, face, and neck and white hairs on the frontal part of the scalp and eyebrows.

Klauder[22] (1930) reports a patient who had been a draftsman during World War I. He had approved specifications of troopships which were not seaworthy and was blamed and threatened with criminal prosecution. On the night before the investigation began, he was away from home in a hotel. He shaved in the evening, as was his custom, and left in the morning without looking at his hair. Upon arrival in the office, his fellow workers exclaimed, "Your hair is snow white." Before the change of color, his hair had been dark brown. There was no alopecia.

Canuto (assistant of Dr. Vignolo-Lutati[40]) observed a woman, 20 years old, who became gray suddenly after a grave disappointment. Seven months later the former color of her hair returned.

Just last year, Erich Hoffmann,[20] of Bonn, reported four cases, which he heard of from physicians, concerning people who suffered overnight graying after catastrophies.

GROUP B (Persons who became gray rapidly while under treatment for neurological or mental disorders).—Exact histories are given.

Landois[23] (1866) tells of a man, 43 years old, hospitalized with delirium tremens and under strict observation, who spoke in a delirium of fear, and appeared extremely tense and frightened. One morning the color of the hair of his head and beard had changed to white. Microscopic examination showed that most hairs were white from root to tip; some were white only in the lower part; some were blond in the lower part and had a gray tip, and some were speckled. The pigment was completely intact over the whole length of hair. On the white part there were many air bubbles, especially in the medulla, but also in the cortex. With transillumination the hair appeared dark in the white areas, in reflected light it appeared white. The air bubbles could be expelled by placing short pieces of hair in warm water, ether, or turpentine. One could observe how the absorbed fluid expelled the air and the hair turned back to the original blond color. Otherwise the hair was completely normal.

Raymond[33] (1882) reports the case of a woman 38 years old who after a succession of exciting and depressing events suffered terribly from neuralgia of the head. The pains became so severe that the diagnosis of acute meningitis was considered. On the fourth night the pain reached a climax. At

2 a. m. the hair was still normal; at 7 a. m. it was completely discolored. The original dark color was still present at the sides and in the back; the front was flaming red, the rest was white or white and red. The hair of the body was not affected. Two days later the red hair turned white. After two weeks the patient lost all her hair, except on the sides and the back of the head.

Heinecke[17] (1904) tells of a woman, 21 years old, with dementia praecox, under observation in a mental institution, who developed during seizures, a streak of white hair, 3 cm. wide, reaching from the forehead to the left side. The hair resumed its normal blond color after four days. The same discoloration recurred with later attacks. Microscopic examination of these white hairs showed more air bubbles in the medulla than found in normal hair. After immersion in water, the air escaped and the hair regained its normal color.

Hoff[19] (1954) presents the case of a miner, 40 years old, under medical observation for chalicosis, who was well and working as a foreman on March 13, 1953, at 2 p. m. Two hours later he complained of a headache, which became gradually worse. At 6 p. m. a minor mine accident was reported to him, and he had to attend to it. Nobody was hurt, and it was a routine job. At 6:30 p. m. he had a chill, fainted, and remained unconscious for approximately 30 minutes. Later he felt nauseous and complained of thirst. The diagnosis of "grippe" was made. During the following night his hair became completely white and he lost a great deal of his blond hair. Little by little the hair of his body also turned white and the brown color of his iris also became very light. He lost 25 lb. during one month; libido and potency disappeared. The hearing of the left ear was impaired, and his testes became smaller. Diagnosis: Trauma in the area of the hypothalamus or encephalitis.

Halloppeau and François-Dainville[15] (1909) presented in the Société Dermatologique française a woman, 40 years old, with severe headache of the left side. Her eyebrows and some hair of the scalp and pubic area of the same side had turned white overnight.

Gowers[14] (1901) reports a case of meningeal hemorrhage of the left side due to accident. The patient survived for three days. During this time the right side of his brown beard turned white and in the center was a line of almost black hair. The change in the hair color was authentically observed during his life and after death.

Loer[25] (1913) reports a case of sudden graying of hair and cilia of one side eight days after hemiplegia; Bourneville and Poirrier, after brain tumor; Duncan and Bulkley, after ataxia.

The following five cases are included here as a subgroup. They represent cases of sudden whitening of cilia as reported by ophthalmologists.

Schencke[35] (1873) presents a case of sudden poliosis circumscripta of the eyelashes. Some of the cilia were white at the bottom; others, at the tip.

Gasteiger[13] (1925) reports the case of a nine-year-old boy, suffering from interstitial keratitis, who developed discoloration of the cilia during the course of a few days. Microscopic examination showed much increased air content in the peripheral part of the hair.

Steindorff[38] (1914) tells of a girl, 17 years old, the cilia of whose right eyelid turned white after fright.

Voigt[41] (1906) reports sudden graying of the cilia of the upper eyelid after iridocyclitis.

Hutchinson and Jacobson report graying of the cilia after sympathetic ophthalmia.

It is possible that the above list is not complete, despite my efforts to assemble the pertinent literature. However, I believe that it suffices to show that there are many *reported* cases of rapid whitening of the hair. Moreover, while many of the reports deserve to be treated with scepticism, by no means all can be just "laughed off." There are some relatively recent ones personally observed and reported by dermatologists of unquestioned ability and veracity.

Report of Case

With this as background I venture into this highly controversial and still "mysterious" area and report the following case of a man who experienced complete whitening of the hair of the head, except for a band-like strip over the occiput. This occurrence was personally observed by me to have occurred in not more than six weeks and probably within two to three weeks after an accident.

A white man, 63 years old, was under my care for several weeks for a generalized contact dermatitis and was practically cured. On Friday, June 14, 1957, he was accidentally pushed down a flight of subway stairs. He broke his wrist and hit the back of his head on the steps. He did not feel nauseous or become unconscious and did not miss a day on his job.

On the day after the accident he came to my office with his arm in a cast to be discharged for his skin condition. At this time his hair was dark brown, strong and wavy, grayish at the temples and with some white sprinkling on the top (Fig. 1).

Six weeks later, when I saw him again, his hair was completely white except for a small band of dark hair near the neckline (Fig. 3). He stated that two weeks after the accident he had noticed loss of hair, but he never became bald or showed bald patches. According to the patient (and I have at no time found cause to doubt his trustworthiness), during *the next week* he turned completely white except for the band-like strip on his neck. Members of his family and business associates remarked about it. The final change, which gave the impression of complete whiteness, must have been quite sudden, as his co-workers all commented about it when he came to work on a Monday morning, four weeks after the accident.

Fig. 1.—Spring, 1956. Last picture taken before accident.

Fig. 2.—Sudden whitening of the hair.

Upon close examination, on Aug. 6, his hair appeared soft, white, and straight (Fig. 2). There was a very small percentage of dark hair mixed in with the white. The condition has not changed since he was presented at the Brooklyn Dermatological Society on Oct. 8, 1957.

The microscopic examination of the hair showed no pathologic changes. The pigment was distributed evenly over cortex and medulla in the dark hair. The white hairs were transparent, with clumps of pigment in the medulla. The patient asserts that his hair was never dyed. This is supported by the fact that he already had a few white hairs before the accident occurred and that today he is not concerned about the remaining strip of black hair.

Comment

The strip of dark hair over the occiput of the patient, which is distinctly darker than the previous natural color of his hair, is probably analogous to the hyperpigmentation seen on the border of some leukodermic plaques. In this case the process of whitening took two to three weeks. Although the textbooks regard blanching in a few weeks as being more frequent than more sudden graying, only a few such cases are reported.

It is still not established whether the usual graying process starts at the root or at the tip of the hair or whether the pigmented hair falls out and is replaced by a white one (Bloch [4]). I questioned several hairdressers on this topic. In their opinion

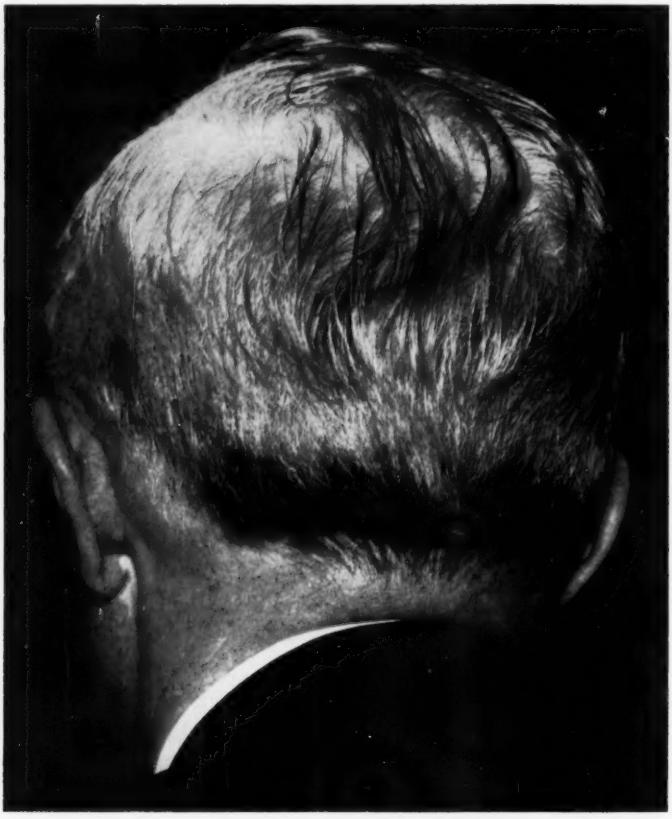


Fig. 3.—Rear view of rapid whitening of the hair.

the pigmented hair turns white at once. They never observed short white new growth but only long white hairs during the physiologic period of graying. This was also observed by Brown-Sequard[6] (1869). When the first white hairs appeared in his beard he pulled them out, only to find white hairs of equal length in the same area the next morning. He repeated this experiment for several weeks with the same result. These white hairs could not in so short a time have grown to the length they presented at the time of plucking.

According to Hamilton, it takes an average of three months for a plucked hair to regenerate and appear at the skin surface. It grows 0.35 mm. daily, or about 1 cm. per month. It thus takes an average of five months for a hair to "regenerate" and to reach a length of 2 cm. This fact alone precludes the possibility of a pigmented hair falling out due to mental stress or accident and being replaced by a white one overnight or in a very short time, such as within a few weeks, as in my patient. The slow growth of hair also negates the explanation that owing to illness or accidents patients forget to dye their hair as usual. Hair dye cannot be removed by water or perspiration alone, and it takes months for the dyed part to grow out entirely. Some men use mascara daily to touch up small areas when the hair is beginning to turn white. Occasional omission to do so may make the hair appear lighter but cannot have the effect of sudden graying of the whole head, as the mascara cannot be used regularly to cover all the scalp hairs in a thick layer.

Theories as to Mechanism of Sudden Graying

Different explanations of the phenomenon of sudden graying or whitening were attempted by Vauquelin and later by Metchnikoff (1901). Vauquelin thought that a mysterious substance, which dissolves the pigment, is excreted under mental stress. Metchnikoff [26] believed that pigment is absorbed and carried away by phagocytes, which he called "pigmentophages." After being saturated with pigment they make their way down through the hair bulb and into the connective tissue, where they deposit the pigment. Both theories have found no support and are practically forgotten.

Landois' theory is that in sudden graying air bubbles enter the hair while the pigment is fully retained. These air bubbles make the hair appear white through light reflection. This theory has been more widely accepted, and the observation has been confirmed microscopically by Heinecke,[17] Gasteiger,[13] Wilson, Knoult, Haxthausen,[16] and Cady and Trotter [7] (in ringed hair). Many still believe the air-bubble theory to be the best explanation, although by some it is accepted only *faute de mieux* ("For want of a better"). Pillsbury holds that the graying may result ". . . from subtle damage to the melanocytes in the matrix so that the hair may lack pigment. Another possible explanation is that stress may induce an alopecia totalis, following which during recovery the hair may lack pigment." However, this mechanism could not account for the *rapid* blanching of the *entire* hair shaft. Today we know that the melanin-producing cells originate from the neural crest. This neurogenic origin may perhaps lead to an explanation of the phenomenon of rapid pigment loss.

The opinion of leading dermatologists of the past and present is greatly divided on this subject.

In France, Brocq believed that one can become gray very fast and even suddenly due to worry and shock. Hallopeau [15] considered these cases as not exceptional, and Dubreuilh [10] believed that whitening can appear rapidly or slowly *d'emblée* without preceding alopecia. Sabouraud and Pignot [34] and Darier consider *le brusque grisonnement comme des légends* ("rapid graying as in legends").

Among Austrian, German, and Swiss dermatologists, Hebra and Kaposi considered it "only possible to turn gray in the period required for the physiological growth of the individual hairs, and therefore neither a single hair nor all the hairs can turn grey other than gradually. In fact they cannot become grey suddenly." Stieda [39] (1910) believed that those who experienced a rapid change of color had been dyeing their hair but had been unable to do so due to illness or excitement. Bruno Bloch,[4] who discovered dopa oxidase and developed the dopa theory of enzymatic melanin formation, expressed doubt regarding the possibility of sudden graying. The same applies of Galewsky, who wrote the chapter on "Hair" in Jadassohn's handbook.

Most American and British dermatologists admit the possibility of sudden change in color of the hair. Ormsby and Montgomery write in their textbook, "Cases of sudden blanching in a single night are sufficiently numerous and well authenticated as among the rare possibilities." Practically the identical words are found in the standard textbooks by Andrews, Hazen, Pusey, Stellwagon, Schamberg, Sequeira, Ingram, and Brain. McCarthy makes a similar statement but with reservations. Sutton and Sutton, on the other hand, believe that physiologic and anatomic facts are incompatible with the possibility of actual nonartificial blanching. Pillsbury and co-workers hold that the ". . . legendary tales of individuals, whose hair turned grey overnight (24 hours) as the result of some crushing, psychic trauma, must be classified in the realm of fiction, despite the reports of otherwise trustworthy observers. Severe emotional stress may cause precipitous greying, but this requires months, not days." McKenna

finds it difficult to believe that there are any means by which the living hair follicles could influence the excreted nonliving exposed shaft. Herman Goodman sees no definitive proof that anyone's hair actually has turned white overnight.

The facts herein reported in the case observed by me are submitted without further comment and as an additional observation. The interpretation of the findings and speculations as to possible mechanism must be left to the reader.

Summary

The question of sudden whitening of the hair is discussed. The reported cases of the last 150 years are cited, together with the views and opinions offered by different textbooks.

Several theories suggested as an explanation are reviewed, and the arguments pro and con are discussed. It is obvious that no satisfactory explanation of the mechanism or the cause of sudden blanching has been developed.

Fig. 4.—November, 1958, after sunburn.

Finally, personal observations are presented of a new case of a man who experienced whitening of most of his scalp hairs in possibly two to three weeks and no more than five weeks after an accident.

27 E. 18th St. (*26*).

Addendum

In Nov., 1958, 17 months after his accident, I had a chance to reexamine the patient, who had just returned from a trip to Florida and looked sunburned. He was worried about the sudden appearance of white spots on different parts of his body.

The patient presented depigmented areas on arms, hands, neck, chest and a few spots over the chin (Fig. 4). In addition there was complete depigmentation of the whole scalp, including the adjacent part of the forehead and behind the ears. The hair was still white, and the dark strip over the occiput was present. There is no doubt that the sudden whitening of the hair was part of an acute vitiligo of the entire scalp. The hyperpigmented borderline fits in with this conception. The white spots had escaped earlier observation due to the very fair complexion of the patient's skin and became visible only after a strong sunburn.

Retrospective close inspection of Fig. *2* shows that there was already a slight color difference of the skin on the forehead. Therefore, it seems obvious that the sudden whitening of the hair in my case—and probably also in many of the previously reported ones—belongs in the group of *vitiligos*. The mechanism of the sudden physiological changes from dark to white hair still remains to be explained.

REFERENCES

1. Behring: Canities der Kopfhaare nach Trauma, Zentralbl. Hautkr. 16:641.

2. Bernard, R.: Les Cheveux peuvent-ils blanchir brusquement? Progr. méd. Paris, p. 1433, 1925.

3. Bichat, M-F-X.: Anatomie générale et descriptive, Paris, 1834, Vol. 4. p. 815.

4. Bloch, B.: Über die Entwicklung der Haut- und Haarpigmente bei Embryonen und über das Erlöschen der Pigmentbildung in ergrautem Haar. Arch. Dermat. u. Syph. 135:57, 1921.

5. Bodin: La Practique dermat, Paris, 1904, Vol. 4, p. 4.

6. Brown-Sequard: Expérience démontrent que les poils pouvent passer rapidement du noir au blanc chez l'homme, Arch. physiol., p. 442, 1869.

7. Cady, L. D., and Trotter, M.: A Study of Ringed Hair, Arch. Dermat. & Syph. 6:301-317, 1922.

8. Cassan: Arch. gén. méd. (Jan.) 1827.

9. Charcot: A propos d'un cas de canitié survenu très rapidement, Gaz. hebd. méd. 8:445, 1861.

10. Dubreuilh: Canitié circonscrite, Bull. Soc. franç. dermat. et syph. 23:480-484, 1912.

11. Feré: Note sur un cas de canitié rapide, Progr. méd. Paris, Vol. 49, 1897.

12. Fischer, F.: Teilweises Ergrauen der Haare nach Trauma, Dermat. Zentralbl. 16:162, 1913.

13. Gasteiger, H.: Über das frühzeitiges Ergrauen von Zilien, Arch. Augenh. 95:261-266, 1925.

14. Gowers: Lancet 2:1173, 1901.

15. Hallopeau, H., and François-Danville: Sur une hémi-canitie d'origine émotive, Bull. Soc. franç. dermat. et syph. 20:395 (Dec.) 1909.

16. Haxthausen, H.: Pili annulati, Dermat. Ztschr. 24:298, 1917.

17. Heinicke: Neurol. Zentralbl., No. 4, p. 146, 1903.

18. Hoff, F.: Haarkleid und vegetatives System, Deutsche med. Wchnschr. 75:478, 1950.

19. Hoff, F.: Akuter totaler Pigmentverlust, Deutsche med. Wchnschr. 79:284, 1954.

20. Hoffmann, E.: Über das plötzlich Ergrauen durch heftigen Schreck: Canitis subita psychogenica, Ztschr. Haut- u. Geschlechtskr. 22:74-78, 1957.

21. Holzgraefe, A.: Alopecie als Symptom neurohormonaler Erkrankungen, Nervenarzt 18: 134, 1947.

22. Klauder, J. V.: Sudden Whitening of the Hair After Mental Stress, Arch. Neurol. 24:415, 1930.

23. Landois: Das plötzlich ergraute Haupthaar, Arch. path. Anat. 35:575, 1866; p. 113, 1869.

24. Lebar: Case of Sudden Canities, Bull. et mem. Soc. med. hop. Paris, 1916.

25. Loer: Hemicanities bei Hemiplegie, Deutsche med. Wchnschr. 1913.

26. McCleod, J. M. H.: Leucodermia and Leucotrichia After Motor Accident, Brit. J. Dermat. 49:437, 1937.

27. Metchnikoff, E.: On the Process of Hair Turning White, Proc. Roy. Soc. London, p. 156, 1901.

28. Metchnikoff, E.: Étude biologique sur la veilleuse et sur le blanchiment des poiles, Ann. Inst. Pasteur, p. 865, 1901.

29. Naegeli, O.: Beobachtungen beim Ergrauen der Haare im Hinblick auf die zurzeit herrschenden theoretisctien Anschauungen, Schweiz. med. Wchnschr. 63:1328, 1933.

30. Parry: Dublin M. Press, 1861, p. 332.

31. Pohl-Pincus, J.: Das Haar, ed. 5, 1905, p. 133.

32. Rayer: Traité des maladies de peau, 1835, Vol. 3, p. 733.

33. Raymond: Rev. Med., p. 770, 1882.

34. Sabouraud and Pignot: Canities, Nouv. prat. dermat. Paris 7:223, 1936.

35. Schencke: Arch. Dermat. u. Syph. 5:137, 1873.

36. Schmidt, M.: Arch. path. Anat. 156:190, 1899.

37. Schoenhoff, A.: Canities praematura acuta, Zentralbl. Hautkr. 10:641.

38. Steindorff: Vitiligo der Lider, Klin. Monatsbl. Augenh., Vol. 53, 1914.

39. Stieda: Wien. med. Wchnschr., Vol. 13, 1910.

40. Vignolo-Lutati, C.: Canizie precoce e psicopatia di guerra, Policlinico 25:680, 1918.

41. Voigt, A.: Frühzeitiges Ergrauen der Cilien und Bemerkungen über den sogenannten plötzlichen Eintritt dieser Veränderungen, Klin. Monatsbl. Augenh., 1906.

42. Voigtel, F. G.: Handbuch der pathologischen Anatomie, Halle, Hemmerde u. Schwetschke, 1804, Vol. 1, p. 90.

Methoxsalen in the Treatment of Vitiligo

An Appraisal of the Permanency of the Repigmentation

JOSEPH A. ELLIOTT Jr., M.D., Charlotte, N. C.

Introduction and Purpose

It has been shown that methoxsalen will enhance the ability of vitiliginous skin to repigment with prolonged exposure to sunlight, the effectiveness varying with the area of skin involved and with the intensity of treatment.[1-12] Assuming that 100% repigmentation will be attained if treatment is continued long enough and with sufficient intensity, then the question arises as to the permanency of this repigmentation. Must treatment be continued indefinitely, or can it be stopped when the degree of repigmentation is satisfactory and the skin still retain the new pigment? Previous reports have not been concerned with this aspect of the treatment of vitiligo with methoxsalen.

The purpose of this study was to answer this practical question within the limits imposed by the period of time methoxsalen has been available for clinical trial and the availability of records and of patients for follow-up examinations.

Material and Methods

This study consists of the determination of the retention of new pigment in 4 patients with vitiligo first treated with methoxsalen in 1954 and 12 additional patients treated subsequently who had sufficient treatment to produce a significant degree of repigmentation and were available for follow-up examinations after a lapse of five or more months without treatment.

Treatment during the summer of 1954 consisted of (1) 10 mg. methoxsalen given orally three times a day after meals; (2) exposure of the depigmented areas to sunlight at noon each day, increasing the time of exposure as tolerated; (3) avoidance of foods with a high ascorbic acid (vitamin C) content (tomatoes, peaches, cabbage, oranges, and grapefruit). Treatment during the remaining period of study consisted of (1) 20 mg. of methoxsalen given daily two hours before exposure to ultraviolet light; (2) exposure of the depigmented area to sunlight at noon each day or, in some cases, a G. E., R. S. sunlamp in the winter or when sunlight was not available, increasing the time of exposure as tolerated.

In determining the degree of pigment retention, each patient was examined with both daylight and a Wood's light and the areas of involvement compared with color photographs of these same areas taken before and after the completion of each period of treatment. The maximum degree of repigmentation and the per cent of this repigmentation retained after a period without treatment were determined. These figures refer to area rather than intensity.

A second phase of this study consisted of evaluating the status of the vitiligo after a period of continued treatment with methoxsalen but with use of a R. S. sunlamp in place of sunlight. Two additional patients who did not meet the criteria for the first phase were included with four of the above patients.

Results

The results of this study are shown in Table 1, together with the age of the patient at the time treatment was initiated, the number of months of treatment, and the period which had elapsed without treatment when the per cent of new pigment retained was determined.

Nine areas on five patients became completely repigmented. Of these areas, only four (two patients) retained 100% of the new pigment after eight months without treatment. In contrast, three areas on another patient lost all of their pigment in 13 months without treatment. Two partially repigmented areas on two patients retained 100% of their new pigment after 8 and 16

Submitted for publication July 14, 1958.

Read before the 78th Annual Meeting of The American Dermatological Association, Inc., Sun Valley, Idaho, June 4, 1958.

TABLE 1.—*Per Cent Repigmentation and Persistence of This Pigment After an Interval Without Treatment*

Case	Age, Yr.	Mo. of Treatment	Repigmentation		Mo. Without Treatment	New Pigment Retained	
			Area	%		Area	%
6	45	4	Face,	50	7	Face,	75
			axillas,	75		axillas,	90
			wrists	25		wrists	90
		9	Face,	75	29	Face,	75
			axillas,	90		axillas,	75
			wrists	35		wrists	0
7	28	4	Face,	50	8	Face,	0
			back,	50		back,	50
			thighs, ant.	90		thighs, ant.	0
			thighs, post	75		thighs, post.	10
			legs	90		legs	10
		8	Face,	75	29	Face,	0
			back,	30		back,	0
			thighs, ant.	75		thighs, ant.	0
			thighs, post.	90		thighs, post.	10
			legs	75		legs	10
8	34	7	Chest	15	29	Chest	10
1	10	6	Fingers	75	28	Fingers	90
2	9	2	Legs	75	28	Legs	90
9	38	4	Face & neck,	25	25	Face & neck,	1
			hands	50		hands	0
3	23	10	Face,	90	23	Face,	0
			axillas,	90		axillas,	90
			forearms,	100		forearms,	75
			hands	50		hands	0
10	41	8	Axillas	25	19	Axillas	75
11	21	8	Axillas	85	16	Axillas	100
12	44	5	Face,	100	13	Face,	0
			neck,	100		neck,	0
			forearms	100		forearms	0
13	35	5	Legs	15	8	Legs	75
14	33	5	Face	60	8	Face	75
		10	Face,	70	8	Face,	75
			axillas	25		axillas	50
15	28	4	Shoulder,	100	8	Shoulder,	90
			forearm,	90		forearm,	100
			chest,	50		chest,	15
			thighs	100		thighs	100
		30	Face,	100	8	Face,	100
			shoulder,	100		shoulder,	100
			forearm,	95		forearm,	100
			chest,	80		chest,	90
			thighs	100		thighs	100
4	37	4	Face,	90	8	Face,	10
			axillas,	100		axillas,	100
			elbow	60		elbow	90
5	44	15	Face,	99	7	Face,	75
			hands	10		hands	75
16	46	3	Face,	100	5	Face,	75
			forearms	25		forearms	20

months, respectively, without treatment. Eight patients were followed for 19 to 29 months after treatment was stopped. None retained 100% of the new pigment in a partially or completely repigmented area.

There was no apparent extension of the vitiligo during treatment. However, partial repigmentation did not prevent further extension of the vitiligo after treatment was stopped.

Although the two youngest patients had 90% retention of their new pigment after more than two years without treatment, there does not appear to be any correlation between age and pigment retention in the other patients. There is no consistent correlation between the interval without treatment and the retention of pigment. Case 1 and Case 2 retained 90% of the new pigment in areas which were 75% repigmented on

Fig. 1.—Patient before treatment. Reproduced with permission from Elliott.[10]

Fig. 2.—After four months of treatment. Reproduced with permission from Elliott.[10]

the fingers and legs, respectively, for 28 months without treatment. Case 3 retained 90% in the axillas, 75% on the forearms, and none on the face or hands after 20 months without treatment. Case 4 retained 100% of the new pigment in her axillas, 90% on the elbows, and yet only 10% on the face after eight months without treatment.

Case 5 developed 99% repigmentation with four months' treatment and retained 75% of this pigment seven months after treatment was stopped (Figs. 1-3).

Fig. 3.—After seven months without treatment.

Table 2 gives the per cent of the areas of vitiligo retaining 75% or more of the pigment and 10% or less of the pigment after various periods without treatment.

There is no significant correlation between the degree of pigment retention and the duration of the disease, extent or area of involvement, or maximum degree of repigmentation.

Six patients continued treatment with methoxsalen during one or more winters, using a R. S. sunlamp for ultraviolet light. Two showed slight continued improvement; one maintained the previous gain in pigment, whereas, three patients showed a slight loss of the repigmentation. Treatment was as vigorous as it had been in the summer with sunlight, but in no instance did the patient maintain the previously attained degree of tan or rate of repigmentation, although the loss of pigment was not as great

TABLE 2.—*Summary of Persistence of Repigmentation*

Mo. Without Treatment	Areas	Patients	75% or Greater Retention, %	10% or Less Retention, %
5-8	28	8	68	21
13-20	9	4	44	56
25-30	13	6	29	68

as during a similar period without treatment.

Comment

Some physicians, in determining what is to be done for a patient, are prone to overlook the latter's perspective of a disease and to discard the need for treatment of any disease which has cosmetic implications only. The patient who avoids social intercourse because of the appearance of his vitiligo is overemphasizing the importance of his disease, but it is that important and serious to him, just as some teen-agers avoid social activities and adversely alter their personalities because of their acne. Thus, any significant repigmentation of vitiliginous skin is of tremendous value to the patient's morale and justifies treatment. This is particularly true of Negroes, who are extremely concerned about any abnormal change in their skin pigmentation.

Although the present method of treatment of vitiligo with methoxsalen is not entirely satisfactory and has many shortcomings, it is still the most effective modality yet reported. Although none of the patients whom I have treated have become completely repigmented, 67% have stated that the results justify the time and money expended.[12] The more information we have regarding the effectiveness of treatment, the persistence of the pigment, and the side-effects of the drug, the better we can inform the patient and select the proper ones for treatment, with a resultant increase in the per cent of treated patients with a "satisfactory" result.

We have learned that the hands and feet do not repigment readily and that those patients who have their major involvement in either or both of these areas are not good candidates for this method of treatment. We also have learned that vitiliginous areas do not repigment in a few days or weeks, but require months of intensive treatment with methoxsalen and exposure to sunlight, and that patients who cannot devote a minimum of 30 minutes near the middle of each day to sun exposure are poor candidates for treatment. We should select our patients for treatment with these facts in mind and then tell them that a satisfactory degree of repigmentation will require at least one and probably two or more summers of treatment and that after a satisfactory degree of repigmentation is attained they will need to continue treatment on a "maintenance" basis indefinitely. If they accept these conditions, then I feel certain that the results will be satisfactory to both the patients and the physician.

The presently available sources of artificial ultraviolet light are a poor second when compared with sunlight as to effectiveness. There is a real need for a source of artificial ultraviolet light of the proper wave length and intensity with a cost within the means of the average patient, so that treatment can be carried out at the convenience of the patient at any time of the day and during the winter when adequate sunlight is not available.

Illumination with a Wood's light increases the apparent contrast between vitiliginous and normal skin and aids in evaluating the extent of vitiligo and persistence of repigmentation when the normal skin is poorly tanned.

There are still some questions which must be answered if methoxsalen is to be used over a long period of time in a given person. Will methoxsalen prevent or promote carcinogenesis? Animal studies[13,14] have indicated the latter, although there is evidence in humans to suggest the former, and large-scale studies are being conducted in Texas in an effort to answer this question.[15,16] What effect does methoxsalen have on light sensitivity? Most evidence points to protective properties due to an increase in the stratum corneum, development of a stratum lucidum, and retention of melanin.[17-19] However, after treatment of their vitiligo with methoxsalen, two of my patients have developed, for the first time, a polymorphous light eruption which has continued to recur with exposure to sunlight after methoxsalen treatment was stopped.[12,20] What chances are there of liver

damage from use of methoxsalen? At least one patient has developed evidence of liver damage while taking methoxsalen, although the relationship is not definitely established.[12]

Summary and Conclusions

Although, when last observed after 8 to 16 months without treatment, three patients had retained 100% of the new pigment in six areas, none of eight patients observed longer than 16 months after treatment was stopped retained 100% of the new pigment in any area. Repigmentation of vitiliginous skin due to methoxsalen and exposure to sunlight is probably not permanent.

Treatment probably must be continued indefinitely, although its intensity can be reduced to a maintenance level once the desired degree of repigmentation is attained.

Vitiliginous areas which become completely repigmented do not seem to retain this pigment any better than areas which are not completely repigmented.

There is no apparent correlation between the degree of pigment retention and the age of the patient, duration of the disease, extent or area of involvement, or maximum degree of repigmentation.

A sun lamp is not as effective as sunlight in repigmenting vitiliginous skin, but it is a valuable adjunct in treatment when sunlight is not available.

Photographs before and after each period of treatment are important in evaluating the progress of the patient.

Suite 706, Doctors Building, 1012 Kings Drive.

REFERENCES

1. El Mofty, A. M.: A Preliminary Clinical Report on the Treatment of Leucodermia with Ammi Majus Linn., J. Roy. Egyptian M. A. 31: 651 (Aug.) 1948.

2. El Mofty, A. M.: Further Study on Treatment of Leucodermia with Ammi Majus Linn., J. Roy. Egyptian M. A. 35:1 (Jan.) 1952.

3. Sekla, M.: Treatment of Vitiligo, Correspondence, A. M. A. Arch. Dermat. & Syph. 65:358 (March) 1952.

4. Sidi, E., and Bourgeois-Gavardin, J.: The Treatment of Vitiligo with Ammi Majus Linn., J. Invest. Dermat. 18:391 (May) 1952.

5. El Mofty, A. M.: Observations on the Use of Ammi Majus Linn. in Vitiligo, Brit. J. Dermat. 64:431 (Dec.) 1952.

6. Lerner, A. B.; Denton, C. R., and Fitzpatrick, T. B.: Clinical and Experimental Studies with 8-Methoxypsoralen in Vitiligo, J. Invest. Dermat. 20:299 (April) 1953.

7. Couperus, M.: Ammoidin (Xanthotoxin) in the Treatment of Vitiligo, California Med. 81:402 (Dec.) 1954.

8. George, W. M., and Burks, J. W., Jr.: Treatment of Vitiligo with Psoralen Derivatives, A. M. A. Arch. Dermat. 71:14 (Jan.) 1955.

9. Kanof, N. B.: Newer Knowledge of Melanin Pigmentation and the Treatment of Melanin Disturbances in the Skin, New York J. Med. 55: 3103 (Nov. 1) 1955.

10. Elliott, J. A., Jr.: The Treatment of Vitiligo with 8-Methoxypsoralen, South. M. J. 49:691 (July) 1956.

11. Sheldon, S. A.; Harrell, E. R., and Curtis, A. C.: Results in the Treatment of Vitiligo with 8-Methoxypsoralen, A. M. A. Arch. Dermat. 74:9 (July) 1956.

12. Elliott, J. A., Jr.: Clinical Experiences with Methoxsalen in the Treatment of Vitiligo, presented at Brook Lodge Symposium on Methoxsalen, Augusta, Mich., March, 1958.

13. Griffin, A. C.: Methoxsalen in Primary Tumors of Mouse Skin, presented at Brook Lodge Symposium on Methoxsalen, Augusta, Mich., March, 1958.

14. Urbach, Frederick: Methoxsalen in Primary Tumors of Mouse Skin, presented at Brook Lodge Symposium on Methoxsalen, Augusta, Mich., March, 1958.

15. Macdonald, E. J.: Methoxsalen in Primary Skin Tumors in Man, presented at Brook Lodge Symposium on Methoxsalen, Augusta, Mich., March, 1958.

16. Hopkins, C. E.: Field Trial in Skin Cancer Prophylaxis: Progress Report, presented at Brook Lodge Symposium on Methoxsalen, Augusta, Mich., March, 1958.

17. Becker, S. W., Jr.: Effect of 8-Methoxypsoralen and Sunlight on Pigmentation and Skin Structure, presented at the Fourth Annual Cosmetic Seminar, Sept., 1957.

18. Becker, S. W., Jr.: Histologic Changes in Human Skin Following Psoralen Therapy, presented at Brook Lodge Symposium on Methoxsalen, Augusta, Mich., March, 1958.

19. Zimmerman, M. C.: Basic Histologic Changes Following Methoxsalen, presented at Brook Lodge Symposium on Methoxsalen, Augusta, Mich., March, 1958.

20. Elliott, J. A., Jr.: Clinical Experiences with Methoxsalen in Suntanning, presented at Brook Lodge Symposium on Methoxsalen, Augusta, Mich., March, 1958.

ABSTRACT OF DISCUSSION

DR. CARL T. NELSON, New York: Experience has shown that the ingestion of 8-methoxypsoralen, together with repeated exposures to natural or artificial ultraviolet light, can induce pigment formation in some areas of vitiligo. However, the response is very erratic, and satisfactory clinical repigmentation probably can be obtained in no more than 1 out of every 7 to 10 cases treated.

At the present time, I believe that most dermatologists would agree that this form of treatment for vitiligo is somewhat less than satisfactory. Moreover, we do not know what the general effects of prolonged or repeated ingestion of psoralens will be, just as Dr. Elliott has pointed out.

Dr. Elliott's study has emphasized many of the important factors to be considered in assessing the value of this type of treatment for vitiligo. Regarding the permanence of any repigmentation obtained after psoralen therapy, he has shown that not only does this vary from patient to patient but also the retention of pigment varies considerably from area to area in the same person. Apparently, if patients with vitiligo treated in this fashion are followed long enough after therapy has been discontinued, practically all of them will show ultimate loss of pigmentation.

The mechanism of action of the psoralens in producing pigmentation under the influence of ultraviolet light and sunlight is not well understood. Lerner and his co-workers have postulated that it is the combined effect of sulfhydryl oxidation by 8-methoxypsoralen and ultraviolet stimulation of melanocytes which results in melanin formation (*J. Invest. Dermat.* 20:299, 1953). On the other hand, as Dr. Elliott has mentioned, Becker (*Science* 127:878, 1958) has shown that the initial reaction of the skin to 8-methoxypsoralen and sunlight is a thickening of the stratum corneum and the formation of a stratum lucidum. The combination of ultraviolet light and 8-methoxypsoralen results in a slight amount of new pigment formation in treated areas, but the pigment is mainly in the basal and horny layers. The pigment-forming cells and their dendritic processes are not filled with melanin, and Becker concludes, therefore, that while 8-methoxypsoralen increases the pigmenting effect of ultraviolet light, the development of the psoralen tan is due primarily to the retention of pigment in the skin.

In addition, we still do not know why certain areas of vitiligo are completely resistant to psoralen and light therapy, while others seem to respond rather readily. There is now some evidence, I believe, to suggest that there may be several biologic variants of the clinical entity we call "vitiligo."

Although it has been shown that melanocytes are not completely absent in vitiligo, there may be a type of this disease akin to albinism, if you will, in which there are virtually no pigment-forming cells with intact tyrosinase activity. In this case, treatment with the psoralens could not reasonably be expected to be effective.

In other instances, the vitiligo may be less absolute, with the melanocytes reduced in number or with their tyrosinase activity diminished. In this type, repigmentation would be possible as a result of stimulation or unblocking of the tyrosinase systems of the remaining melanocytes.

I think that these differences in response of different areas of vitiligo to psoralen therapy demand explanation, and, perhaps, further histochemical studies will help us predict which types of vitiligo warrant a trial of 8-methoxypsoralen therapy.

In closing, I might say that it had been our impression that the incidence of good responses to 8-methoxypsoralen treatment in vitiligo is related to the duration of the vitiligo. We have felt that the older cases are less responsive to this type of treatment, and I am interested to learn that this impression was not borne out in Dr. Elliott's study.

DR. THOMAS B. FITZPATRICK, Portland, Ore.: Most of us have been discouraged with the treatment of vitiligo with furocoumarins, and yet Dr. Elliott's results indicate a significant and perhaps therapeutically worthwhile repigmentation of vitiligo with the combined treatment of methoxsalen and sunlight.

Over the past five years we have treated 123 patients with vitiligo using oral methoxsalen. In our series, only a small fraction, approximately 15%, obtained a result that could be considered cosmetically acceptable enough to justify the prolonged, tedious treatment required. One of Farber's patients has repigmented almost 90% of the depigmented skin with use of methoxsalen over a period of three years. This patient was exposed to sunlight in large part, obtaining it first in the Azores and later in California. However, even under ideal conditions of optimum dosage and prolonged exposure to sunlight as a source of ultraviolet, I have had several patients who gave up the treatment because of incomplete repigmentation, etc. Until better methods of treatment of vitiligo become available, I believe that we are justified, particularly in view of Elliott's results, in giving the vitiligo patient a trial of three to six months of oral methoxsalen with sunlight exposure. This is especially true in the pigmented peoples (Asiatic, Indian, and Negroid) who have severe cosmetic disfigurement.

I know that many of you have been concerned with the toxicity of methoxsalen. I have not seen any serious toxic effects of methoxsalen in over

six years of experience in hundreds of patients and volunteer subjects. We have this past year examined the question of hepatic toxicity, using a carefully designed blind study. This is being reported in *The Journal of the American Medical Association*. Daily ingestion of 30 mg. for a period of three months in normal medical students did not reveal a single instance of hepatic toxicity as detected by a battery of hepatic tests, including the sulfobromophthalein (Bromsulphalein) dye test. This study is not conclusive, however, since a series of 450 patients would be required to prove the negative effect of a drug. Recently, one of the large pharmaceutical companies reported to me a study of 120 patients treated with 20 mg. over a two-week period without detectable change in the hepatic tests.

There are other questions besides the one of hepatic toxicity. Are these agents carcinogenic? Injection of huge doses (almost 50 times the clinical doses) intraperitoneally into albino mice and followed by exposure to 15 minutes of high-intensity ultraviolet radiation (sufficient to produce erythema on normal Caucasian skin in 10 seconds) results in the production of cancers, predominantly fibrosarcomas. These experiments are difficult to interpret, since the conditions are so far removed from the ones used in man. Also, the mice are albinos. Nevertheless, they should make us vigilant for any possible precancerous effects in vitiligo and other patients using methoxsalen. Furocoumarins are found in edible foods and have been used in crude form as far back as 1,000 B. C., and methoxsalen has been given to thousands of patients over the past 10 years in Egypt, France, Mexico, and the United States. There have been no reports of carcinomas in these patients. A rather large double-blind trial which now includes 145 patients is going on in one of the sunniest parts of this country to test the hypothesis that oral methoxsalen may *decrease* the incidence of solar-induced keratoses and carcinomas. This trial has been carefully designed, and the patients are being followed by excellent clinicians. Perhaps in a year or so we will have some answers.

DR. JOSEPH A. ELLIOTT JR., Charlotte, N. C.: I should like to reemphasize two things about the treatment of vitiligo with methoxsalen. First, in patients with involvement primarily of the hands and feet, the results of treatment do not justify the cost or the time involved. Second, I am sure that the further south one goes the more effective the treatment is, as a result of more hours and greater intensity of the sunlight; and so I think that our result, in comparison to that of Dr. Nelson, is in direct relationship to the difference in latitude.

Skin-Marking Technique

JOHN van de ERVE, M.D., Charleston, S. C.

A simple and easy method of marking the skin is desirable and often needed in dermatological practice. The marks should not be soluble in water or alcoholic solutions and should persist for several days. In the past, I have used wax skin-marking pencils, such as are commercially available, and also indelible-ink ball-point pens. Previous marking methods included silver nitrate, gentian violet, Bonney's blue, and even scratching the skin itself. All of these disappear rather rapidly under friction from clothing, detergent action, and perspiration.

An interest in oil painting led to an acquaintance with the felt-nib pen that artists use for sketching. For the past year I have been using this pen for marking the skin. On looking into the matter I found that Tamerin and Bornstein,[1] in 1950, published a short article on the use of this type of pen and the aniline dye, oil-based, which it uses. The ink is self-sterilizing. It is composed of a light distillate base comparable to high-grade naphtha or kerosene. The gums, waxes, and resins in the ink are those used in the pharmaceutical trade in the manufacture of ointments, cerates, and emulsions. The black ink uses an aniline dye. The ink adheres well, dries quickly, and does not dissolve in alcohol or water. Acetone, benzene, and nail-polish remover dissolve it quickly and easily remove it from the skin.

The Flo-Master pen supplied by Cushman and Dennison Company* and the Marsh 77 Felt-Point Pen (Marsh Stencil Machine Co.)† were used during the past year for patch testing and marking on some 400 patients. I found no reaction of any kind in this series. The regular black transparent ink was used. In addition, the Flo-Master Special Skin-Marking Ink was tested. No reactions were found. In the process of manufacture of these inks, where contact is more frequent and intense than in any casual use, there were only a few rare cases of irritation.

Tamerin and Bornstein[1] used a sterile metal quill-tip pen and wooden holder when using the ink for preoperative work. This would be useful in preparing a patient for abrasion or planing for marking both the bases of the scar pits and for outlining fields for abrasion. I have been using the felt pen particularly to mark plant resin patch-test sites, where it often persists for two to five days, except in hot weather. It is excellent for marking glass microscope slides and glass containers of any kind in the laboratory, for outlining areas for vibrapuncture, and for making signs and notices about the office. It adheres on metal surfaces as well.

180 Wentworth St.

Submitted for publication July 31, 1958.

Clinical Professor and Department Head, Department of Dermatology, Medical College of South Carolina.

*Cushman and Dennison Co., New York 11; Flo-Master Hospital Marking Pen and Inks.

†Marsh Stencil Machine Co., Belleville, Ill.; Marsh 77 Felt-Point Pen and Ink.

REFERENCES

1. Tamerin, J. A., and Bornstein, L. A.: A New Type of Skin Marking Ink, Plast. & Reconstruct. Surg. 6:475-478, 1958.

2. Nabatoff, R. A.: Importance of Adequate Excision of All Incompetent Perforator Vessels in Surgical Treatment of Varicose Veins: Use of New Marking Ink to Delineate Varices, New York J. Med. 52:563-565 (March) 1952.

3. Flo-Master Marking Pen and Inks, New York, Cushman and Dennison Company.

4. Marsh 77 Felt-Point Pen and Ink, Belleville, Ill., Marsh Stencil Machine Company.

The New, Newer, and Newest

The most heartening bit of news in many a day was the information that there is now a National Foundation for Research in Cutaneous Medicine, Inc. It is a nonprofit organization designed to promote and support research in the "vast and neglected" field of skin diseases. The Foundation plans also to provide an intensive educational program for the general public on the subject of skin diseases. The President and Executive Director is Mr. Louis L. Spirt, 370 Lexington Ave., New York 17. Frank Combes, a member of the Foundation's Board of Trustees, is also a member of the still-incomplete medical advisory board, which includes, so far, Beinhauer, Harvey Blank, Callaway, Arthur Curtis, Dobes, Mescon, Muller, Osborne, Rattner, Reisch, Rothman, and Sulzberger. Long overdue, this organization should have the blessing and complete support of all dermatologists.

The Academy meeting, in December, was again big, busy, bustling, and altogether enjoyable. I was able to attend only a small part of the meeting, but reports are as follows:

The most exciting announcement of the meeting was the restrained report by Harvey Blank and Frank Roth on the treatment of superficial fungus infections with Griseofulvin, a new orally administered antibiotic preparation, fungistatic to certain organisms. The impact of the report was so great that, by popular request, it was repeated on the next day in the large ballroom in order to accommodate everybody—something that has never before occurred at an Academy meeting. Incidentally, the drug is not yet available.

This ARCHIVES hopes to publish the full report soon.

The sessions were so much better where speakers used notes.

The surprisingly large attendance at the sections on "Physiology and Chemistry of the Skin," "Internal Medicine in Relation to Dermatology," and "Psychosomatic Aspects of Dermatology." The usual full attendance at the bread-and-butter sessions, such as "Industrial Dermatoses," What's New," "Hand-Eczema," "Cutaneous Surgery," "Malignancy," etc., and the very small groups listening to "Socioeconomic Aspects of Dermatologic Practice."

The banquet was excellent and entertainment most entertaining—one of the best parties in years.

A topic brought up for discussion at almost every round-table meeting was the vexing problem of the loss of hair in women, for no apparent reason.

Assurances by various speakers with regard to x-ray therapy in dermatology.

The visitors from abroad were amazed and pleased by the Academy's accent on youth.

Mr. Carl Herzog, of Duke Laboratories, long an anonymous benefactor of the Academy, has donated $10,000 to promote the educational program of the Academy. Time to uncover the anonymity.

Prize-Winning Exhibits

Class I, for Original Work

The Gold Award to Moretti, Montagna, and Mescon, Boston University and Brown University: Blood Vessels of the Human Skin.

The Silver Award to Paul Hirsch and Elson Helwig, Armed Forces Institute of Pathology: Mixed Tumor.

The Bronze Award to Victor Wheatley, University of Chicago: New Methods for the Study of Human Skin Lipids.

Class II, Exhibits of High Teaching Value

The Clyde Cummer Gold Award to George Prazak and John Ferguson, Brooke Army Medical Center: Superficial Fungus Infections.

The Silver Award to Charles De Feo, Maurice Costello, and Marvin Dannenberg, New York University-Bellevue Medical Center: Pemphigus—Diagnosis, Types, and Treatment.

The Bronze Award to Harry Shotin, Orlando Canizares, and Emory Ledany, Veterans Administration Hospital, Bronx, N. Y.: Reiters Syndrome and Keratosis Blennorrhagica.

The newly elected officers of the Academy are as follows:

Anthony C. Cipollaro—President

Norman McK. Wrong—Vice-president

Bob Kierland, Stanley Huff, and Sam Zakon retain their respective offices as Secretary,

Assistant Secretary, and Historian.

Edward Cawley was elected to represent the Academy on the American Board of Dermatology to succeed John Lamb.

Thomas Butterworth, C. Ferd Lehman, Walter Lobitz, Francis Lynch, and Walter Shelley were elected to the Board of Directors for three-year terms and Don Birmingham to fill the unexpired term of the late James Webster.

Honors

Earle D. Osborne, Professor and Head of the Division of Dermatology at the University of Buffalo, received a citation from the University ". . . a leader with triple-genius for research, teaching and administration . . . man of heroic stature in medical education." Hear! Hear!

On Rostrums Here and There

Marion Sulzberger will deliver the Pusey Lecture for the Chicago Dermatological Society on March 18. The subject: "Ruminations on American Dermatology; Whence? Where? Whither? and Not Forgetting, Why?"—a timely talk in the light of Blank's report.

John R. Haserick, March 3, 1959, for the Annual Clinical Conference of the Chicago Medical Society on "What to Do About the Unexpected Positive Serologic Test for Syphilis."

Aaron B. Lerner, Jan. 20, 1959, for the Eighth Annual Sigmund Pollitzer Lecture, sponsored by the New York University Post-Graduate Medical School, on "The Pituitary, Pineal and Pigmentation."

Louis Brunsting, Nov. 11, 1958, for the Interstate Post-Graduate Medical Association, in Cleveland, on "Juvenile Eczema."

George Andrews, Oct. 23, 1958, for the Southwestern Medical Association, on "Common Dermatoses of the Hands."

Adolph B. Loveman, Oct. 18, 1958, for the Kentucky-Tennessee Regional Meeting of the American College of Physicians, at Louisville, on "Mucous Membrane Lesions."

Earle Osborne, Nov. 3, 1958, for the Omaha Mid-West Clinical Society, in Omaha.

Coleman Mopper, Nov. 19, 1958, for the Mexican Society of Dermatology, in Mexico City, on "Sarcoidosis" and "Alopecia Mucinosa," both delivered in Spanish, which he learned for the occasion.

Looking after things for the

Canadian Dermatological Association:

R. R. Forsey, Montreal, President; J. F. Daily, Burlington, Vt., Vice-President; and G. E. Craig, Montreal, Secretary.

Brooklyn Dermatological Society:

Morris Rothstein, President; Benjamin Bender, Vice-President; and Lawrence Frank, Secretary.

Connecticut State Medical Society, Dermatology Section:

Ellwood C. Weise, Jr., Bridgeport, President, and Cleveland R. Denton, Hartford, Secretary.

Mexican Dermatological Society:

Conception Estrada, President; Fernando Latapi, Secretary; Manuel Malacara, Assistant Secretary, and Josefa Novales, Treasurer.

From Newspaper Reading

Radiologists exposed to limited amounts of radiation in their daily work live slightly longer, on the average, than do other medical men, etc., etc.

A mystery rash spread all through West Germany—hope the victims do not turn red!

"Dermatologists Elect"—A. Fletcher Hall, Santa Monica, Calif., as President of the Pacific Dermatological Association.

Voodoo dolls, imported from Haiti, with heads carved from cashew-nut shells for use as swizzle sticks, "may inflict blistering skin reactions."

Scientists Want Small M.D in Orbit by '60. How about John Lamb?

Bennett Cerf's amusing one about the mouse used for various scientific experiments. The mouse was placed in a missle that went into orbit. Three months later, the nose cone was retrieved and the mouse restored to its cage at the scientific laboratory. Other mice immediately surrounded him and excitedly asked, "Tell us, how did it feel to be in orbit?" The mouse shrugged his shoulders and nonchalantly replied, "Well, it's better than cancer!"

H. R.

Correspondence

LARVA CURRENS

To the Editor:—I was most interested to read in the A. M. A. Archives of Dermatology 78:186, 1958, the article on larva currens.

Recently, I have tried treating larva migrans with Trafuril applied locally. I find it an effective remedy, and the results are sometimes dramatic. In other cases, however, it does not work, and I wondered if these were, in fact, cases of Strongyloides infection.

Trafuril (CIBA) is tetrahydro-furfuryl nicotinic acid ester, which is exhibited as a 5% rubefacient cream and is normally used to relieve muscular rheumatism, lumbago, etc. It may perhaps kill the larvae directly or alternatively sweep them away in the resulting hyperemia.

I feel this drug is worthy of further trial in creeping eruptions, as in my experience it is at least as good as freezing with ethyl chloride and considerably easier to apply.

G. H. N. Clarke, M.D.
Senior Specialist (Dermatology)
General Hospital
Lagos, Nigeria, West Africa

Society Transactions

LOS ANGELES DERMATOLOGICAL SOCIETY

S. W. Becker, M.D., President
Floralou Kettenbach, M.D., Secretary

May 14, 1958.

Cheilitis Glandularis Apostermatosa (Volkmann). Presented by DR. CLEMENT E. COUNTER.

A 22-year-old Caucasian man has had a tender, swollen lower lip for the past 10 years. The onset was at the age of 11 years. First aware of lip distress when he was convalescent from tonsillectomy. The lip gathers a sticky, yellow crust when no ointment is used. Wintertime brings some relief of symptoms. His father and grandfather had the same lip disease in a milder form. Neither his brother nor his sister have this condition.

Present Examination.—Lower lip is prominent. It is greased with an emolient, yet scales are present. There are two palpable nodules present. A clear, stringy discharge gathers in droplets on the lower lip when it is palpated.

Previous Treatment.—Seven x-ray treatments of 75 r each—total 525 r in Beaumont Army Hospital with no apparent relief of symptoms; 5% "sulfa salve" locally; vitamin D ointment locally; injections of preparation of identity unknown to patient.

Present Treatment.—An ointment containing ichthyol with hydrocortisone 1% in Lassar's paste (Naftalan). Two weeks after using this prescription, observation showed the lip doing very well and remaining well for 12 hours after the ointment is removed.

Microscopic Examination of Biopsy Specimen.—Epiderm is deficient over much of the section. Where it is present it has lost its interpapillary pegs, and much of the sharpness usually present in the germinative layer is gone. The cutis is very vascular, and between fibrous trabeculae are packed round cells almost entirely filling the upper part of the dermis. At least one round patch of looser lymphocytes is formed among the denser grouped cells to resemble a germinative center of a lymph node. This is close under the epiderm.

Discussion

DR. NORMAN E. LEVAN: In addition to the lip lesion, this patient has both systemic and other cutaneous indications strongly indicative of lupus erythematosus. According to the history, the lip condition has since its onset been aggravated by sunlight and accompanied from time to time by other light-sensitive lesions, on the malar areas chiefly. At present there are erythematous tumid areas high on the cheeks and on the wings of the nose. In addition, since the onset the patient has been unable to compete physically with his fellows because of easy fatigability and weakness and episodes of malaise. As brought to my attention by Dr. Jud Scholtz, he shows arcus senilis—certainly significant of a systemic disorder when found in a 22-year-old man.

In the microscopic sections there are no glandular changes to bear out a diagnosis of cheilitis glandularis apostermatosa. The dense nests of lymphocytes are, of course, consistent with lupus erythematosus. I have seen a similar lip involvement with similar histologic changes in what, following the lead of Jessner, we have been calling lymphocytosis cutis. It may well be that some instances of this morphologic entity are variants of lupus erythematosus, and with the strong adjuvant evidence present in this patient I would hesitate to suggest an alternative diagnosis until the possibility of lupus has been thoroughly investigated.

As to therapy, antimalarials are indicated at present.

DR. J. WALTER WILSON: Almost everyone here knows what I am going to say. When I see a lower lip involved on the exposed surface of the mucous membrane in the central portion only, sparing the corners of the mouth very definitely and not spreading over onto the cutaneous surface below or onto the inner true mucous membrane, it is difficult for me to accept the diagnosis of lupus erythematosus. It is true that this patient might have lupus erythematosus, and some of the lesions on the nose actually suggest it, but I should like to see some evidence of it from a biopsy specimen taken from the nose area before I accept that diagnosis. I think this man has what Hiram Miller called "mouth breather's plaque." I saw him cure at least five cases like this simply by telling the patient to wear a chin strap at night. These

Submitted for publication June 19, 1958.

persons breathe through the mouth at night, licking the lower lip frequently with the tongue, and allowing the saliva to evaporate. These plaques all look like this man's—in the central portion of the lip. I think a chin strap would cure this man.

DR. HAROLD PRICE: Cheilitis glandularis apostematosa is thought to be possibly of congenital orgin and is due to adenomatous hyperplasia of the mucous glands. There is also associated dilation and hypertrophy of the ducts. Secondary infection may complicate the picture.

In this case, the section showed no evidence whatsoever of glandular structures, and, therefore, I doubt very much that this is cheilitis glandularis.

DR. SAMUEL AYRES JR.: I think it is cheilitis actinica, and there is such an entity. It is possible to have an inflammatory condition of the exposed part of the lower lip from sun sensitivity without having any manifestation elsewhere on the skin, and the patient seemed to be very definitely certain that this condition was worse in the summertime. A physician cousin of mine had the same thing, only his was particularly troublesome out of doors on vacation. He wore a protective shield over his lips while fishing. I suppose that this man has had the benefit of a sun-screening lipstick. If he hasn't, that type of protective measure should be used, and I should certainly second the idea that chloroquine or one of the other antimalarials be used.

DR. SAMUEL AYRES, III: I think cheilitis glandularis is a clinical entity. True, he doesn't show the enlarged glandular openings which one associates with it, but he gives a definite history of a glairy secretion when the lips are put together and then separated. This condition has been going on for a long time and with the amount of crusting that he has it is no longer possible to demonstrate it. However, I still think this is a very good possibility and that the presenter's diagnosis is correct.

DR. CLEMENT E. COUNTER: When I first saw this patient he had an acute exudative process involving the lower lip. On palpation a clear stringy secretion appeared in bead-like droplets at about eight different points on the lower lip. Also palpation showed three indurated lumps. One of these was excised for the biopsy specimen presented tonight.

Squamous Cell Epithelioma. Presented by DR. JEROME K. FISHER for therapeutic suggestions.

A 33-year-old Caucasian man has been married for eight years and has five children. The patient had "jungle rot" while in service but no serious illness. He had two disks in his back removed two years ago. He never had any venereal diseases.

The patient was circumcised in 1949 because of a constricted prepuce. Although he was not aware of any lesions on the glans penis, he did notice some "red areas" develop there within about nine months. These were asymptomatic. For the past five years he has been treated for what he says is "psoriasis." He has had several biopsy specimens taken, but he does not know the exact diagnosis. For the past three years warty growths have appeared over the glans penis.

The eruption is confined to the glans penis mostly near the coronal margin, leaving the tip near the meatus free. The lesions are verrucous and confluent. They are tender to palpation. No nodes are palpable in the groins. He has no other cutaneous eruptions except some mild scaling over the scalp.

Biopsy findings showed squamous-cell epithelioma, Grade 2. Blood Wassermann test is negative.

No treatment has been given by the presenter. Patient has received solid carbon dioxide (Dry Ice) twice and five or six x-ray treatments elsewhere in 1956.

Discussion

DR. LAURENCE J. UNDERWOOD: The treatment of this carcinoma, I believe, should be carried out by a surgeon. It is of interest only secondarily to theorize what dermatosis preceded the present keratotic, verrucoid nodular plaques. One may speculate as to whether erythroplasia or balanitis was present in the past. It is doubtful that he has had psoriasis localized on the penis for years without other evidence of psoriasis elsewhere. It would be a mistake to temporize by considering the lesion a verruca or other benign lesion.

DR. J. WALTER WILSON: This particular class of carcinoma is similar to that which was called verrucous carcinoma by Ackerman in his textbook of surgical pathology, the recent edition. We saw one like this intraorally, and it looks so much like a wart that one begins to wonder whether it is actually malignant or not, and yet it does invade tissues very deeply if given a chance.

DR. MURRAY ZIMMERMAN: I think if this man is fairly well preserved that I would suggest chemosurgery. The mortality rate for carcinoma of the penis is the highest of any skin cancer, not because it is a different type of carcinoma, but because doctors and patients alike are unwilling to treat it adequately. There is a characteristic history of "too little and too late" on the carcinoma of the penis. Chemotherapy as practiced by Mohs would be able to remove this with an absolute minimum loss of normal tissue.

DR. LOUIS H. WINER: Ackerman's carcinoma shows proliferation of the epidermal rete, such as one sees in condyloma accuminatum and also without inflammatory reaction in the cutis. The lesions are usually localized to the mouth. This patient has a Grade 2 squamous-cell carcinoma. This penetrates deeper than does early erythroplasia of

Queyrat. Erythroplasia of Queyrat localized to the skin of the penis and glans is easily removed by desiccation or simple excision of the lesion. When the mucous membrane at the meatus of the urethra is involved, it is more serious and rapidly metastasizes to the regional lymph nodes.

DR. SAMUEL AYRES: I don't see any strong contraindication to giving intensive fractionated doses of x-ray as given for skin carcinomas, with a resulting minimal sacrifice of tissue. The Mohs technique is also good, but I don't think that it has to be a choice between it and super-radical excision or amputation as the only other alternative. I think that adequate intensive x-ray should be given and that it could be in the hands of the dermatologist.

Cultures from a Case of Tinea Capitis Due to Trichophyton Ferrugineum. Presented by DR. GAGE HELMS.

This is a case report of a 4½-year-old Korean-American orphan brought to this county in October, 1957, and adopted by a couple in this vicinity. It is stated that this patient on arrival had scaly patches over the scalp. The foster parents consulted a family physician, and a diagnosis of tinea capitis was made. Therapy has consisted of the local application of several of the popular fungicidal preparations.

Examination of the patient's scalp reveals a scaly, circular, noninflammatory condition over approximately 75% of the scalp. Examination under Wood's light reveals a fluorescence of the hair in the scaly areas. Cultures were presented. This is probably only the third or fourth time this organism has been isolated in the United States.

Discussion

DR. J. WALTER WILSON: We all read about rarities in the texts and literature, but we have not yet seen all of them. A common cause of ringworm of the scalp in the Far East and the Balkan Area is said to be Trichophyton ferrugineum. We have had cultures of this organism sent to us for teaching purposes for many years but have never had the opportunity to obtain one from an involved patient directly. These brilliant yellow cultures grow very slowly for a long time. Dr. Helms told me that this child had the infection of the scalp while still in Korea and that the organism in culture was not typical of any of our common fungi. I asked him to send it to me, and I sent it on to Dr. Plunkett, the mycologist from University of California at Los Angeles, who is a guest here tonight. He will tell you what he thinks of it.

DR. ORDA A. PLUNKETT (by invitation): This culture is undoubtedly similar to the ones we have always studied as T. ferrugineum. The only culture we have had before came from one of the two cases observed by Dr. Lewis, in New York, some years ago on Chinese children. The only other report of this organism having been isolated in this country came from San Francisco—also on a Chinese child. I have never seen a good account of this organism anywhere. It produces a faviform type of colony, with little early aerial mycelium. After a few weeks the surface of the colony becomes raised, roughened, and lighter yellow in color. The characteristic feature that one sees under the microscope is the mycelium composed of irregular bead-like cells and enlarged vesicles in which there is considerable granular content. Most of the granules are yellowish in color. The color of the colony is due to the colored granules in the vesicles. The organism is very distinct, and I think without doubt is T. ferrugineum.

DR. JEROME K. FISHER: I should like to ask Dr. Plunkett as to treatment for this sort of thing. Does it behave like Microsporum audouini?

DR. ORDA A. PLUNKETT: Well, I understand the infected hairs fluoresce, and it resembles an infection of the audouini type with little or no erythema or scaling. As to treatment, I don't know. I have not seen any published results of treatment for it at all. How well it responds to local topical medication, I don't know.

Case for Diagnosis: Acrodermatitis Enteropathica Sine Enteropathica? Presented by DR. MAXIMILIAN E. OBERMAYER and DR. CHARLES GEORGE STEFFEN, (by invitation).

Pemphigus (Face and Groin). Presented by DR. PAUL D. FOSTER.

Lupus Erythematosus vs. Pseudopelade. Presented by DR. MAXIMILIAN E. OBERMAYER.

(1) Palmar and Plantar Arsenical Keratoses; (2) Right Palm Ulceration-Bowenoid Epithelioma; (3) Right Palm-Secondary Moniliasis of Ulcer and Right Ring and Little Finger Paronychia and Nails. Presented by DR. LAURENCE J. UNDERWOOD.

Adenoma Sebaceum (Pringle) with Peri- and Subungual Warty Fibromas. Presented by DR. THEODORE M. COHEN.

Eczema? Presented by DR. ANKER K. JENSEN.

Case for Diagnosis: Sarcoid Reaction. Presented by DR. JOHN A. HOSMER and DR. MARGARET ANN STORKAN.

Lymphoma? Prurigo? Presented by DR. BEN A. NEWMAN.

NEW YORK DERMATOLOGICAL SOCIETY

J. Lowry Miller, M.D., President
Frank E. Cormia, M.D., Secretary

Jan. 28, 1958

Trichophyton Rubrum Infection of the Nails.

Presented by Dr. Maurice J. Costello.

A woman aged 30 has had a Trichophyton rubrum infection of the toenails and fingernails for the past six years.

Treatment has consisted of the usual antifungal agents, including Verdefam, and surgical removal of the nails, followed by daily application of Isodine, with recurrence. Numerous antifungal agents have been used conscientiously without avail.

The patient saw a member of this society in consultation and since then has been applying pumice stone and double-strength Whitfield's ointment, without improvement; in fact, the infection has spread to the adjoining fingernails. The patient is presented for suggestions as to therapy.

Discussion

Dr. Carl T. Nelson: These cases are extraordinarily difficult to cure and I have concluded that it is not so much the medication applied to kill the fungus that deserves study as it is the factors in the host that permit this type of parasitism to persist. The infection is rather superficial, but it resists all forms of treatment. What are the host factors in this situation? I think that is the phase that warrants investigation.

Dr. George M. Lewis: At the present state of our knowledge it must be admitted that we can seldom achieve a good result quickly. There are certain basic principles to follow: one is to use some abrasive; another is to apply a succession of fungicidal or keratolytic drugs, and last, to do something, as Dr. Nelson has intimated, to develop host resistance. There is some evidence that vitamin A is useful, and there may be some virtue in a high-protein diet in the hope of increasing the rate of nail growth, which, after all, would theoretically cure these infections. I should here suggest rotation of drugs locally, abrasive preparation before application, and vitamin A and gelatin in large doses.

Dr. J. Lowry Miller: Has Dr. Lewis felt that there is any response to gelatin treatment for nails? I have used it extensively; so far, with negative results. For that reason I am skeptical of its efficacy. The reason I give the patient for continuing to treat the nails is to prevent spread to other areas of the body, and I believe this is justified. Patients who have had the infection for 10 or 15 years quit treatment and then get new lesions on the body. These are rather easily cleared up, and, if the nails are treated, no new lesions appear on the body.

Dr. A. C. Cipollaro: I do treat patients with T. rubrum infection of the nails. I am under the impression that fungicidal preparations and abrasion prevent spread of infection to other parts, prevents paronychia, and improves nail growth. X-ray therapy is of little use in this condition, except perhaps to cause quicker involution of the paronychia. I do not use x-rays for treatment of T. rubrum infection of the nails. The present-day tendency is to use x-rays less for benign conditions, and this is one in which we can do very well without them.

Dr. George C. Andrews: I wonder whether we want to subscribe to Dr. Cipollaro's remarks that dermatologists no longer use roentgen ray therapy, except in malignant tumors. Is that the general impression? This fungous infection might not respond to x-ray therapy, but on the other hand, a few doses might do a great deal of good and would not do any harm. X-ray therapy should not be used if it is not necessary, but in this condition it would not be harmful. The patient has involvement of the skin of the sole, and one has to exfoliate the skin to get rid of the fungous infection because it is often deep in the epidermis. I should advise exfoliating agents, as has been suggested, and I should go after that rather vigorously. I doubt that you would get the nails cleared without treating the skin of the foot rather vigorously, and if you get that cleared and give fractional doses of x-rays to the remaining nails, it would offer a good prospect of cure.

Dr. George M. Lewis: It is my opinion that x-rays are contraindicated for the treatment of fungous infections of the nails because the effect is to inhibit the rate of nail growth. It is also well known that even a large dose of roentgen rays has no discernible effect on fungi.

Dr. George C. Andrews: I have never seen nail growth retarded.

Dr. Maurice J. Costello: Of all the skin diseases I treat, the most inveterate is T. rubrum infection of the nails. I used to send patients to surgeons for removal of the nails until I realized that they just remove the nail. More recently, I have removed the nail and scraped the bed with a curet under the folds, abraded the area around it, and did as thorough a job as anyone could do, short of injuring the matrix. Someone asked why

we used Isodine. I once heard it said that if iodine were applied after the removal of a nail, it would increase the rate of cure. I have removed all 10 nails, using iodine postoperatively only on one hand, which became cured while the other did not. Isodine is supposed to be just as effective as iodine from that point of view. Still, we cure very few of these cases. This patient was seen by Dr. Lewis in consultation. He suggested abrasive treatment, with double-strength Whitfield's ointment, and the patient carried out the treatment conscientiously. As far as gelatin is concerned, I am not impressed. I shall try some of the methods suggested, but I feel this is one of the biggest problems in dermatology, and it is a very frequent occurrence in my practice.

Bad Results from Planing in the Treatment of Freckles. Presented by Dr. George M. Lewis.

A woman, aged 35, consulted a dermatologist in September, 1955, for advice in regard to freckles on the arms, chest, and back. She received about 20 planing treatments between September, 1955, and June, 1956. The patient is disappointed in the result and would willingly return to her pretreatment status if that were possible.

The affected skin shows various degrees of depigmentation and some irregularities of the surface. Areas of atrophy and scarring are present.

Questions to be considered are as follows:

1. Will there be further improvement (the last planing was over one and one-half years ago)?

2. Is there any value in peeling the skin chemically?

3. What is the best current advice as to masking preparations—potassium permanganate? Shake lotions? Covermark?

4. What advice should be given regarding exposure to sunlight?

Discussion

Dr. Wilbert Sachs: If we want to show failures from planing, there would be no meeting where we couldn't have at least several cases. The failure here is mild compared to others I have seen. As far as this case is concerned, I do not think the pigment will come back. In the second place, the operator went beyond the epidermis, so there is little chance of the pigment coming back. I think sun tanning would only stand out more.

Dr. J. Lowry Miller: The sequelae are worse than the freckles. If any exposure to the sun is given, the part that has been planed is certainly not going to tan as the rest of the skin will, so the patient will be very unhappy.

Dr. L. P. Barker: I have not used planing for the removal of freckles, and I do not believe it should be used for this purpose. This patient exemplifies the fact that removing freckles on the body by planing is very likely to produce scarring. I do not believe normal pigmentation will return in the treated areas.

Dr. A. N. Domonkos (by invitation): That was a demonstration of the fact that planing is not a suitable means of therapy for any part of the body other than the face. Planing on the back or arms will invariably produce atrophic scarring, and there is no hope for these cases. As with so many procedures, there are those who try planing for all sorts of conditions—moles, nevus flammeus, etc. In my opinion, the only indication for this mode of therapy is for scars on the face.

Dr. A. C. Cipollaro: This is a poor result. I believe that the scarring, atrophy, and depigmentation are permanent. The cosmetic effect is worse than the freckles. I doubt if this patient can ever again expose herself to the sun. I should be very much disinclined to recommend surgical planing for the removal of freckles on the chest, back, and arms. Even mild planing for the treatment of scars and freckles frequently leads to permanent depigmentation and some atrophy. Surgical planing destroys tissue and should be used very discriminately. I must admit that I am not enthusiastic about surgical planing. It is of limited usefulness.

Dr. Frank E. Cormia: I am inclined to agree for the most part with Dr. Domonkos. Generally speaking, the follicles are much fewer on the back than on the face, which makes the possibility of scarring infinitely greater on the back. I do not feel as pessimistic as Dr. Cipollaro and Dr. Sachs; I believe patients are moderately improved with facial planing. I do not think one necessarily gets pigmentary difficulties on the face, and I have not produced more than one or two small scars. I do not go that deep. To get the best results you have to be a little courageous, and I am conservative. I think you can improve the contour of acne scars with a reasonably good over-all effect.

Dr. Orlando Canizares: I think we should limit the discussion to this particular case. I agree entirely with Dr. Domonkos; planing of the face is different from planing the chest or arms. I realized, myself, in the only case I tried that I was getting a different feeling from what I got on the face, and I have never done it again. The results obtained on those areas are different from those obtained on the face.

Dr. M. J. Costello: I do not think Dr. Cipollaro's remarks should be deleted. If these discussions are published in the Archives they may help to bring about a more conservative and realistic approach to dermabrasion. We should approach the American Academy of Dermatology.

DR. GEORGE C. ANDREWS: A great many reputable and outstanding dermatologists do planing and believe the results are worth while. We realize that this patient has been improperly treated. All here agree that they would not use planing on the chest, back, or arms but only on the face. We have seen the results from sandpapering and planing, and I have some patients who are very grateful, so I think it is unreasonable to say it should never be used. I think there is some merit in the statement that the teaching at the American Academy of Dermatology has been overextended, and some young men will use the procedure as a panacea. It is difficult for the Academy to arrange these courses. The men who do the teaching are overburdened. The older men have too much to do, and the younger men are unreliable. I believe it is wrong to use planing on everything, and too much should not be expected from it. Some cases are unimproved, but if it is used carefully and by someone with experience, I believe that most are improved and some remarkably. It is certainly a worth-while procedure.

DR. GEORGE M. LEWIS: I am concerned over the management of this problem, as the patient is emotionally upset about the whole episode and requires careful handling. I do not think she is suicidal, but she is very much depressed. I had in mind instructing her carefully about sun-screening and warning her not to go out into the sun without some protection in order to avoid accentuation of the disfigurement. Perhaps some of the hyperpigmentation can be reduced by a weak solution of sodium hyposulfite. I hesitate to suggest Benoquin for this patient. Also, a dilute solution of potassium permanganate may be useful to hide the depigmented areas. I thought it was peculiar that so much planing was done when it must have been obvious after the first treatment that it was not going to be sucessful. Perhaps a more symmetrical effect was obtained by going ahead with so many treatments. I think Dr. Domonkos put his finger on the important thing. We should confine dermabrasion to the face, with few exceptions: for instance, seborrheic keratoses often respond well. The final results of planing for acne scars are very good and much better than after trichloroacetic acid or carbon dioxide slush.

Chronic Disseminated Discoid Lupus Erythematosus. Presented by DR. GEORGE C. ANDREWS.

A white housewife, aged 54, was in good health until 10 months previous to this writing, when she noted a crusted, whitish lesion on the bridge of her nose. A biopsy specimen, July, 1957, was reported as acanthoma. Lesions appeared on the upper lip and chest, and these were treated by electrodesiccation. These lesions recurred, and others developed on the dorsa of the hands. A biopsy specimen taken in October, 1957, was reported as lichen planus.

In the past the patient has had pleural effusion with possible empyema, followed by whooping cough and measles with subsequent kidney infection. In adult life her health has been good except for some hypertension. There is also a history of severe sunburn when she is exposed to the rays of the sun.

The lesion involves a good deal of the nose with marginal erythema and a thick crust covering most of the lesion. The lesions on the left cheek and upper lip have involuted since treatment was begun. There are sharply circumscribed, erythematous patches on the sternum and the backs of the hands.

Urinalysis was normal, with porphyrins not detected. A blood cell count showed hemoglobin 14.1 gm. and white blood cells 6,200, with neutrophils 53, eosinophils 2, lymphocytes 40, and monocytes 5. The platelets numbered 183,000. The sedimentation rate was 6 mm. in 1 hour. The blood urea nitrogen was 12 mg.; total proteins were 6.4 mg., with albumin 4.5 mg. and globulin 1.9 mg. The nonprotein nitrogen was 25 mg. The L. E. test was negative. The VDRL reaction was negative. Roentgenograms of the chest showed no active pulmonary disease, and the heart shadows were not remarkable.

Treatment has consisted of chloroquine, 250 mg. b. i. d., since Dec. 23, and lesions on the nose, cheek, upper lip, and parts of the lesions on the sternum have had several injections of Meticortelone suspension. The total amount injected has not exceeded 25 mg. at any one time. There has been considerable improvement.

Discussion

DR. WILBERT SACHS: I should disagree with the diagnosis of lupus erythematosus, although there is a very strong resemblance. I should like to see a biopsy specimen from the back of the hand, because the eruption there, with a few lesions from the chest, made me think she might possibly end up with lichen planus.

DR. L. P. BARKER: I think this is a case of lupus erythematosus. In this stage they must be watched very carefully because they may develop the acute disseminated form.

DR. A. C. CIPOLLARO: I agree with the diagnosis of lupus erythematosus, but I can not understand the histologic diagnosis of keratoacanthoma. I did not think there was any resemblance histologically between lupus erythematosus and keratoacanthoma, although I know the latter bears a strong resemblance to squamous-cell epithelioma.

DR. ORLANDO CANIZARES: I agree with the diagnosis and should like to ask Dr. Andrews

about local injections of Meticortelone and how they compare with local injections of chloroquine.

DR. M. J. COSTELLO: I believe the patient had local injections of Meticortelone and simultaneous internal administration of the antimalarial drugs. The lesion on the nose I should consider to be the hypertrophic form, which is notoriously hard to cure. It is still present. I believe the resolution of the erythema surrounding these hypertrophic lesions was effected by the antimalarial drugs administered.

DR. GEORGE C. ANDREWS: The patient had been under the care of a number of dermatologists, and the eruption had been misdiagnosed. There were two biopsies performed, the pathologist had reported lichen planus, and the patient had received a great deal of x-ray therapy, during which the eruption became worse. When I saw the patient in consultation I telephoned her dermatologist and told him it was a case of lupus erythematosus, that I was afraid she was getting a disseminated type and thought she ought to be admitted to Presbyterian Hospital for a complete medical study, including an L. E. test. I think an error in the pathologic diagnosis led the dermatologist astray. It is fortunate that she has not got a positive L. E. test.

DR. G. F. MACHACEK: When a clinician is called into consultation, he sees the patient. If you want the pathologist's intelligent decision, you should let him see the patient also. It might make a big difference.

DR. WILBERT SACHS: Could you possibly get the slide diagnosed as lichen planus and let Dr. Machacek look at it?

DR. GEORGE G. ANDREWS: I shall try to.

DR. G. F. MACHACEK: There are instances where it may be exceedingly difficult to differentiate between lupus erythematosus and lichen planus on the basis of the histology alone.

DR. A. N. DOMONKOS: This case was not presented as a response to treatment with Meticortelone, though we have treated a number of cases of discoid lupus erythematosus with that drug, with a favorable response. One member commented that these cases, especially the hypertrophic type, are recalcitrant, and in those we have used Meticortelone with success. You can not expect to get involution with one injection. The lesions on the cheek and upper lip which did not have crusting have responded to perhaps two injections. The one on the face has not responded as rapidly.

DR. M. J. COSTELLO: What influence did you think the internal medication had?

DR. A. N. DOMONKOS: Aralen was given internally, 500 mg. daily. The erythema of the hands is much less.

Pustular Bacterid. Presented by DR. GEORGE C. ANDREWS.

A business woman, aged 52, has had a pustular eruption for the past 10 years, and for the past 6 years she has been under my care for treatment of the hands and feet. During this time her palms and soles were intermittently so severely involved that she was unable to conduct her business. She has had no other eruptions. The lesions of the palms and soles have consisted of small pustules with exfoliation and fissures. This patient is a diabetic under good control.

Roentgenograms of the teeth in 1952 showed a devitalized lower right cuspid with no periapical infection, with incomplete root canal filling. In 1952, the tonsils were noted to be considerably enlarged, with slight inflammation. Repeated examinations for fungi during the past six years have been negative. Urinalyses have been normal with the exception of occasional glycosuria. The white blood cell count has been around 14,000, with normal differential counts.

Despite the severe episodes of the disabling eruption on the palms and soles, repeated urging that she have a tonsillectomy was of no avail until Nov. 6, 1957, when the operation was performed. Her family physician wrote: "The tonsils were hyperplastic and manifested disease. On grasping them, pus was expressed. The microscopic examination showed chronic tonsillitis. Her skin condition has improved markedly. My congratulations on your diagnosis and correlation of the two conditions."

There has been a steady improvement of the palms and soles since her tonsillectomy, 10 weeks ago.

DR. WILBERT SACHS: I should like to see the patient again in two months to see if all lesions are gone.

DR. L. P. BARKER: The result of therapy is very good so far. There is still a great deal of scaling and hyperkeratosis on the soles. If this is the same process, and I assume it is, it should also clear.

DR. A. C. CIPOLLARO: Frankly, I should have difficulty in making a diagnosis of anything on what I saw tonight. If the patient had come into my office, I should have had to consider the diagnosis of psoriasis, or a Trichophyton rubrum infection. Pustular psoriasis or pustular bacterid would not occur to me at present because of the complete absence of lesions. I understand the patient did have lesions of that type prior to tonsillectomy.

DR. M. J. COSTELLO: I agree with the diagnosis, both from the photographs and from what the patient presents tonight. She is not well yet but greatly improved. The eruption may take a long time to disappear.

Melanoma (of 30 Years' Duration?). Presented by DR. CARL T. NELSON.

A man, aged 59, first noted a black spot on his left heel in 1928. This slowly grew but was not treated until 1937, when the lesion was removed by electrodesiccation and curettage, followed by wide local excision. The site healed uneventfully. In 1947, another "black wart" was noted on the left heel in the area of the previous excision. This was again removed surgically. Recurrence of "black spots" at the site of excision was again noted in 1955. Since then, additional pigmented areas have appeared in and adjoining the operative site. During the past year a new, black, warty lesion has appeared at the anterior margin of the left heel.

The left heel shows a large operative scar, studded with several darkly pigmented areas. The anterior portion shows a single warty melanotic lesion, 2 cm. in diameter. No popliteal or inguinal nodes are palpable. The physical examination is otherwise not remarkable. The skin is clear elsewhere.

The urinalysis was reportedly normal, with no melanuria. Biopsy of the lesion removed in 1937 was reported as melanoma. Biopsy of the lesion excised in 1947 was reported as malignant freckle.

There has been no recent treatment. Amputation of the left leg at midcalf has been advised.

Discussion

DR. A. N. DOMONKOS (by invitation): The very impressive feature of this case is the fact that it has been of so long duration—at least 30 years. I understand that biopsy reports twenty and ten years ago were all of melanoma, with a possibility of melanotic freckle. These lesions do not appear to be as sharply outlined as you would expect in satellite lesions of melanoma, and in spite of the fact that one must accept the diagnosis, I think conservative treatment would be indicated. On the basis of the thirty years' duration, I should hesitate to advocate amputation of that foot.

DR. CARL T. NELSON: I should like you to take into consideration, in considering the type of therapy, the fact that this man is a barber and must stand many hours each day. There is considerable doubt on the part of the surgeon that enough of the heel would be left after wide local excision to give a functioning foot.

DR. A. C. CIPOLLARO: I feel as Dr. Domonkos does. If it is a melanoma it is progressing extremely slowly. He may live 10 or 20 years longer it it doesn't metastasize. I should be very much inclined to recommend a conservative operation to remove the soft tissues about the foot and graft the area. His own foot would be much more comfortable and useful than an artificial limb.

DR. FRANK E. CORMIA: I wonder whether it could fall into the classification of Hutchinson's melanotic freckle and so be of relatively low malignancy?

DR. ORLANDO CANIZARES: I agree with Dr. Cipollaro; I think it should be excised.

DR. M. J. COSTELLO: I think this lesion represents lentigo maligna; one area is exceedingly black, shading down to yellowish red. The fact that it has been present 30 years shows that it is at least slowly progressive. I should be inclined to do nothing about it or should certainly be conservative in the surgical approach. The last thing I should advise would be amputation of the leg.

DR. GEORGE C. ANDREWS: I think it started as a lentigo maligna, of a very low grade of malignancy, and I believe local destruction would be ample treatment. However, I would prefer, in this case, on the basis of others I have cured, to use electrocoagulation for the reason that if you get a recurrence after electrocoagulation you can see it. It will come back as a lump or a black spot. However, if you hide it with a graft you could not see it early. That procedure would also give a superior result as far as mobility, absence from work, ability to stand on the feet, etc. are concerned. You get a better result from wide and deep thorough electrocoagulation than you get from excision and grafting. This is an unusual case, and I offer an unusual type of treatment for it, but one that I have used successfully for lentigo maligna on the shoulder, face, and other areas.

DR. G. F. MACHACEK: The first section is undoubtedly melanoma; the second is more superficial. However, since that was taken, there has been infiltration. That area has been operated on. This illustrates the fact that you cannot foretell the biologic activity by the morphology alone. What to do is a grave decision, and it should be put up to the patient. I should be in favor of amputation and perhaps excision of inguinal lymph nodes.

DR. GEORGE M. LEWIS: Because of the age of the patient and the protracted course, I should favor conservative therapy. I should advise the patient to refuse an amputation. The surgeons would then find a method to excise that area and fill the defect with a full-thickness graft.

DR. JOHN C. GRAHAM: This man is 59. His last recurrence took 10 years. I should go to Dr. Andrews and have his method of treatment, which I agree with 100%, and I should not have a skin graft. If you have a graft and get a recurrence you do not know it is there. The form of treatment is not necessarily curative, but I think it is so far superior to the possibility of getting a recurrence with an amputation that I can't see that at all.

DR. WILBERT SACHS: If this patient came into my office as he is tonight, I should be very depressed. It would comfort me to know the history.

If there was any question of nevocarcinoma in the early slide, the man would have been dead if it had not been well removed. I saw no nevus cells tonight, but before I would do anything heroic I should want a few more biopsy specimens. No matter what is done I think it should be conservative, and certainly no amputation should be performed, if that second slide is representative of what he has now.

DR. JOHN C. GRAHAM: Why multiple biopsies? Why not all at one time?

DR. WILBERT SACHS: I do not think there would be any harm in taking two or three sections. If they show nevocarcinoma, nothing is going to save him. Could you, Dr. Machacek, see any active cells in that second section?

DR. G. F. MACHACEK: I think so, but superficially, and it was taken some time ago.

DR. CARL T. NELSON: As I interpret the remarks, the members, with one exception, oppose midcalf amputation. I think it is surprising that this group votes, with one exception, for treatment by local excision. The sections have been studied by several competent pathologists, and they agree that we are dealing with malignant melanoma. The disease has gone on for 30 years, and the patient is fortunately still alive. The suggestion now is that he should be treated in the same way that has failed on two previous occasions. I am particularly concerned because I think the surgeon can be persuaded to do just that, even though he feels that the man will have no functioning heel to stand on. From a mechanical point of view, midcalf amputation would seem to be the conservative treatment.

DR. A. C. CIPOLLARO: How many of us have watched for years cases identical to this one? I have followed at least a dozen of them. I should do what I have recommended here—conservative surgery, because there are melanomas that do not kill. This one has not killed him in 30 years.

DR. GEORGE M. LEWIS: I don't agree that previous treatment has failed. The patient is alive. I also feel strongly that the patient should be protected in that he does not realize how serious a disability an amputation would be. I should not want my own leg off under the circumstances.

Eosinophilic Granuloma. Presented by DR. GEORGE C. ANDREWS.

A banker, aged 56, has had a solitary nodule on the left cheek for several months. His past history includes appendicitis, lobar pneumonia, and coronary thrombosis, all of which occurred within three weeks. There is no history of drug ingestion.

On the left malar region there is a plum-colored lesion, somewhat rubbery in consistency, 2 cm. in diameter, which has involuted considerably within the past month since roentgen therapy has been started.

The hemoglobin was 100%; red blood cells, 4,500,00, and white blood cells, 12,500, with polymorphonuclear leukocytes 61, lymphocytes 32, eosinophils 1, basophils 1, and monocytes 1. The platelet count was 270,000.

Biopsy showed a somewhat attenuated epidermis, with several dilated follicles. The cutis was edematous, its dilated vessels surrounded by a striking infiltration of mononuclear leukocytes, among which were many eosinophilic cells. There was also evidence of a polymorphonuclear leukocytic infiltration. The lesion was not a sarcoid, nor was there any evidence of epithelioma. Diagnosis: Eosinophilic granuloma? Leukoblastoma?

The lesion was treated by x-ray therapy, 100 r at 100 kv., unfiltered, at weekly intervals for a total of 200 r. It has greatly improved.

Discussion

DR. A. C. CIPOLLARO: The cutaneous lesions have involuted to a degree where I can not make a diagnosis, and from the response to x-ray therapy and from what I see, I should interpret this as having been a Spiegler-Fendt sarcoid.

DR. FRANK E. CORMIA: The pathologic findings in eosinophilic granuloma are more pleomorphic, while those of Spiegler-Fendt sarcoid are more uniform. I agree with the diagnosis and think the result of treatment is good.

DR. GEORGE M. LEWIS: In a patient we presented many years ago there was an associated Trichophyton rubrum infection. Control of the fungous infection has been synonymous with freedom from tumors. This probably was purely coincidental. However, I wondered whether Dr. Andrews has examined this patient's feet or would with that specifically in mind.

DR. WILBERT SACHS: I do not know what to call some of these isolated lesions occurring on the face or over the sternum. Microscopically, they frequently look like lymphoblastomas—what some call lymphocytomas. In some cases they are called eosinophilic granulomas. At times we have suggested comparatively small doses of radiation, and in each case the lesion disappeared. I do not think such a lesion is uncommon, but just what to call it I do not know. I do not think it is a lymphoblastoma, and I do not think it is an eosinophilic granuloma. I believe it is an entity that occurs on the face and sternum.

DR. J. LOWRY MILLER: Within the month I have had a patient with an arcuate lesion very similar to this one, of six months' duration. I did a biopsy and suggested the diagnoses of T. rubrum infection, lymphoblastoma, and sarcoid. Dr. Machacek looked very carefully, and he ruled out sarcoid and suggested possible lupus erythematosus. I gave a fractional dose of x-rays, 75 r, and was wondering

what to do next. The patient came back the next week with the lesion about 60% gone. I gave another dose, and now you cannot see the lesion. Did he have a lymphoblastoma, or what?

DR. GEORGE C. ANDREWS: The future of this patient will give the answer.

(Note: A search was made for T. rubrum, and the organism was found in material from the feet, although it could not be grown from the lesion itself.)

Multiple Phleboliths (Calcinosis?) Presented by DR. GEORGE C. ANDREWS.

Announcements

First Annual Nelson Paul Anderson Prize Essay Contest.—The Los Angeles Dermatological Society, Inc., has established a Nelson Paul Anderson Memorial Fund which offers a $500 cash award annually for a minimum of five years for a winning essay to be read by the essayist at the annual meeting of the Pacific Dermatological Association. The Pacific Dermatological Association will pay the basic expenses (transportation, room, and board) of the winning essayist to, at, and from the meeting.

The essays eligible for this contest will report original work, not previously published, formally presented or previously prize-winning, relative to some fundamental aspect of dermatology.

The essays will be judged on the following considerations: (*a*) originality of ideas, (*b*) potential importance of the work, (*c*) experimental methods and use of controls, (*d*) evaluation of results, and (*e*) clarity of presentation.

The essays should be submitted under a "nom de plume," with no information anywhere in the paper which might lead to the recognition by the judges of the institution or clinic at which the work was done. The essay with "nom de plume" should be accompanied by a plain sealed envelope enclosing the name and address of the author; this envelope will not be opened until the judging is complete.

The contest shall be open only to physicians engaged in the study or practice of dermatology who are working within the geographical limits encompassed by the Pacific Dermatological Association.

The essays will be judged by a committee of five judges, appointed by the Executive Council of the Pacific Dermatological Association, and all entries should be in the hands of Louis H. Winer, M.D., 9915 Santa Monica Blvd., Beverly Hills, Calif., in quintuplicate (all copies clearly legible, of course) before May 1, 1959. The winner will be notified by Aug. 1, 1959; the 1959 meeting of the Pacific Dermatological Association will be held at the La Playa Hotel, Carmel-by-the-Sea, Calif., Sept. 9 to 13, 1959.

you can clear topical infections promptly with

NEO-POLYCIN*

...because Neo-Polycin provides 3 preferred topical antibiotics

NEOMYCIN / BACITRACIN / POLYMYXIN

in the unique Fuzene® base which releases greater antibiotic concentrations than do ordinary grease-base ointments.

NEO-POLYCIN covers the entire range of bacteria most often found in topical lesions...has a low index of sensitivity...averts the risk of sensitization to lifesaving antibiotics, since the antibiotics used in Neo-Polycin are rarely used systemically...is miscible with blood, pus and tissue exudates without loss of efficacy.

Each gram of Neo-Polycin Ointment contains 3 mg. of neomycin, 8000 units of polymyxin B sulfate and 400 units of bacitracin in the unique Fuzene (polyethylene glycol diester) base. Supplied in 15 Gm. tubes. Also supplied as Neo-Polycin Ophthalmic Ointment (anhydrous, lanolin-petrolatum base) in ⅛ oz. tubes.

*Trademark

PITMAN-MOORE COMPANY • INDIANAPOLIS, INDIANA
DIVISION OF ALLIED LABORATORIES, INC.

YOUR
GUIDE TO
CURRENT PUBLICATIONS

Quarterly Cumulative Index Medicus

WITH AUTHORS AND SUBJECTS . . .

Divided into sections, one devoted to books and the other to periodical literature, the QUARTERLY CUMULATIVE INDEX MEDICUS contains a list of current publications alphabetized as to authors and subjects. The exact bibliographic reference is given under the author with titles in the original language, while titles under subjects are all in English. The index also includes a listing of journals, addresses and publishers.

The QUARTERLY CUMULATIVE INDEX MEDICUS appears twice a year; volumes are cloth bound and cover periodicals for six months as indicated on the publication. These two volumes will be a convenient and inclusive reference for current medical literature. Invaluable for practitioners, specialists, teachers, editors, writers, investigators, students and libraries.

SUBSCRIPTION PRICE $25.00 PER YEAR
CANADIAN AND FOREIGN $27.00 PER YEAR

AMERICAN MEDICAL ASSOCIATION
535 NORTH DEARBORN STREET
CHICAGO 10, ILLINOIS

Incorporated in exclusive ACID MANTLE vehicle

Quick Soothing Topical Response

IN INFLAMMATORY DERMATOSES

Cort-Dome™

Acid Mantle-Hydrocortisone

CREME AND LOTION—pH 4.6

ABATES INFLAMMATION AND RESTORES NORMAL SKIN ACIDITY

"Susceptibility to infection by bacteria is widely held to be due to the removal of the antibacterial 'acid mantle' of the skin and its displacement by an abnormal 'alkaline mantle'."—Fabricant, N. D.: A. M. A. Arch. Otolaryn. 65:11, 1957.

Supply—½%, 1% and 2% hydrocortisone in either Creme (½ oz., 1 oz., 2 oz., 4 oz. tubes and 1 lb. jars) or Lotion (½ oz., 1 oz., 2 oz., 4 oz. squeeze bottles and pt. bottles).

Samples and literature available on request.

Dome Chemicals Inc.

NEW YORK 23 • LOS ANGELES 46 • In Canada: 2765 Bates Road, Montreal

ALCOHOLISM

an important problem in today's living!

The following articles from TODAY'S HEALTH are now available in one pamphlet for 50 cents . . .

ALCOHOLICS ANONYMOUS. Written from the standpoint of a member, the basic treatment procedures are described and the psychological problems confronting the alcoholic are discussed.

ALCOHOL AND CIRRHOSIS OF THE LIVER. Relationship between alcohol, diet and cirrhosis. Increasing stress on nutritional differences. by Russell S. Boles

HOW TO HELP A PROBLEM DRINKER. Understanding the alcoholic's capabilities, the necessity of help, causes of his condition. by Edward A. Strecker and Francis T. Chambers, Jr.

THE TREATMENT OF ALCOHOLISM. Tracing the steps from convincing the alcoholic that he is sick through treatment and cure. by Lewis Inman Sharp

CONDITIONED REFLEX TREATMENT OF CHRONIC ALCOHOLISM. Its place among methods of treatment today, its development and correlation with personality factors. by Walter L. Voegtlin

INSTITUTIONAL FACILITIES FOR THE TREATMENT OF ALCOHOLISM. Comparative differences, in drinking, with the last century, new establishments and methods of treatment, lack of trained personnel. by E. H. L. Corwin

other pamphlets available . . .

ALCOHOLISM IS A DISEASE. A discussion by the Chairman of the A.M.A.'s Committee on Alcoholism. by Marvin A. Block, M.D., 8 pages, 15 cents

I AM THE WIDOW OF AN ALCOHOLIC. Three articles combined. by Virginia Conroy, 16 pages, 20 cents

HOW EXPERTS MEASURE DRUNKENNESS. A partial transcript of an actual courtroom case. by H. A. Heise, 8 pages, 15 cents

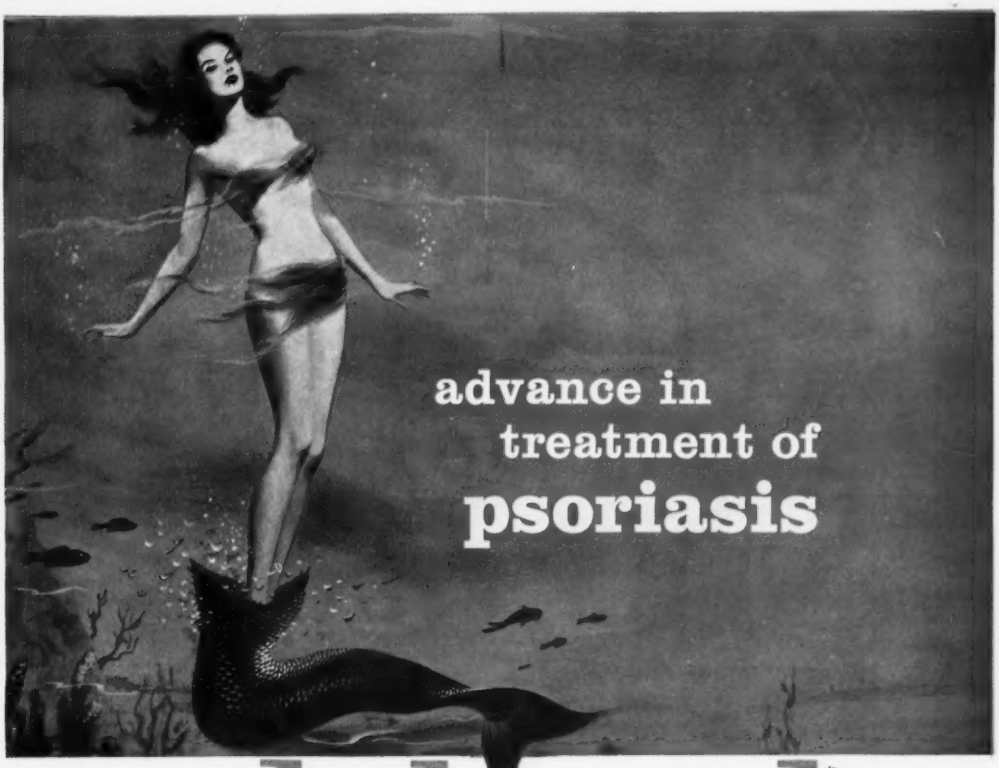
BARBITURATES, BOOZE AND OBITUARIES. A discussion of the dangers of mixing alcohol and barbiturates. by Donald A. Dukelow, 4 pages, 10 cents

TWELVE STEPS FOR ALCOHOLICS. A frank discussion of the meaning of an alcoholic behavior. by Richard Lake, 6 pages, 10 cents

address requests to . . .

ORDER DEPARTMENT

AMERICAN MEDICAL ASSOCIATION
535 NORTH DEARBORN STREET, CHICAGO 10, ILLINOIS



alphosyl*

LOTION

Affords keratin-dispersing action[1]: Keratolytic, removes nonviable tissue, promotes healing.

Successful results ranging to complete clearing obtained[2-4] in patients with: • scalp-to-toe psoriasis • psoriasis of many years' duration • psoriasis involving tender areas.

Treatment-fastness rarely occurs: Recurrences (when treatment is discontinued) clear up again on resumption of therapy.

Well tolerated: Even when applied to lesions in anogenital and submammary regions.[2] Potential hazards of other therapies – mercury, arsenic, corticosteroids, x-rays – are avoided.

A noteworthy advance cosmetically: Nongreasy, nonstaining; vanishes on application to the skin. May be used freely on the scalp.

Application: Rub into lesions 2 to 4 times daily as indicated. Where heavy scaling or crusting occurs, the usual bath, to soften and facilitate removal of scale, is recommended before applying lotion.

Residual redness and pigmentation may remain up to several months but will eventually disappear. Once the condition is under control, daily to weekly application may prove satisfactory for maintenance.

In some cases, a seeming excessive scaling and drying may occur during therapy. This is an occasional phase of the healing process and usually precedes improvement. Patients should be advised of this and encouraged to continue therapy.

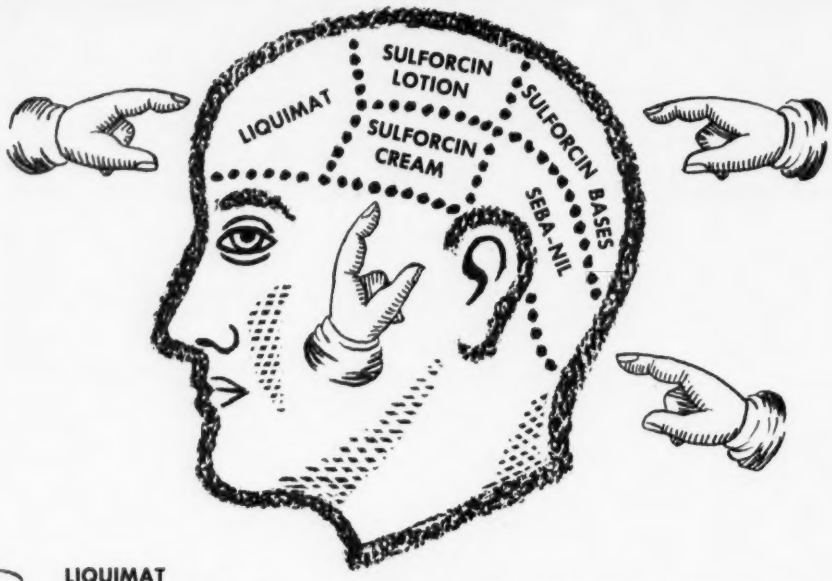
Formula: Allantoin 2% and special coal tar extract 5% in a lotion base.

Supplied: Bottles of 8 fl. oz.

(1) Flesch, P.: Reported Conf. N. Y. Academy Science May 9, 1958 (In Press). (2) Bleiberg, J., and Saltzman, J. A.: Clin. Med. 5:485 (Apr.) 1958. (3) Bleiberg, J.: Reported Conf. N. Y. Academy Science May 9, 1958 (In Press). (4) Clyman, S. G.: Reported Conf. N. Y. Academy Science May 9, 1958 (In Press). *Trademark

R&C **REED & CARNRICK** • Jersey City 6, New Jersey

For ACNE:
keep these effective products in mind



LIQUIMAT

A tinted lotion containing 5% precipitated sulfur for the local treatment of acne. Resorcin, corticosteroids, calamine, phenol, menthol, camphor, betanaphthol and coal tar solution may be added. To individualize prescriptions further, the three shades may be interblended.

SULFORCIN LOTION

Contains 5% dispersible sulfur and 3% resorcinol monoacetate in a colloid-processed base of citrus pectin. Sulforcin Lotion dries rapidly, holding sulfur securely to the skin. Non-sticky, non-greasy, non-staining.

SULFORCIN CREAM

Contains 5% dispersible sulfur and 3% resorcinol monoacetate in a water soluble vanishing cream type base. Lubricating and washable, Sulforcin Cream is especially suitable for application to large areas, and where dryness exists.

SULFORCIN BASES

A greaseless cream type make-up base supplied in 3 strengths and 3 shades which enable you to prescribe precisely for your patients' needs. Sulforcin Base helps conceal blemishes and is an excellent make-up foundation.

SEBA-NIL

Clinical studies prove conclusively that very oily skins respond more rapidly to acne therapy when cleansed with Seba-Nil rather than soap and water. Seba-Nil contains organic solvents and a mild, non-ionic detergent which make it more efficient than soap and water in preparing oily skin for medication.

For detailed information and samples, write

TEXAS PHARMACAL COMPANY

San Antonio, Texas

NYLON NET Full Fashioned Two-Way Stretch ELASTIC STOCKINGS

OPEN TOE—CLOSED HEEL—SEAM BACK—FOR MEN AND WOMEN . . .

EXCELLENT COSMETIC AND THERAPEUTIC VALUE

THIS THERAPEUTICALLY EFFECTIVE ELASTIC STOCKING WITH GRADIENT SUPPORT IS THE ESSENTIAL BEGINNING OF CORRECTING FLUID DYNAMICS AND CAN PROMOTE VENOUS AND LYMPATHIC RETURN OF FLUIDS FROM THE EXTREMITIES.

CUSTOM MADE FROM MEASUREMENTS . . . 24 HOUR SERVICE WHEN REQUESTED

PRICES for 1300 Line

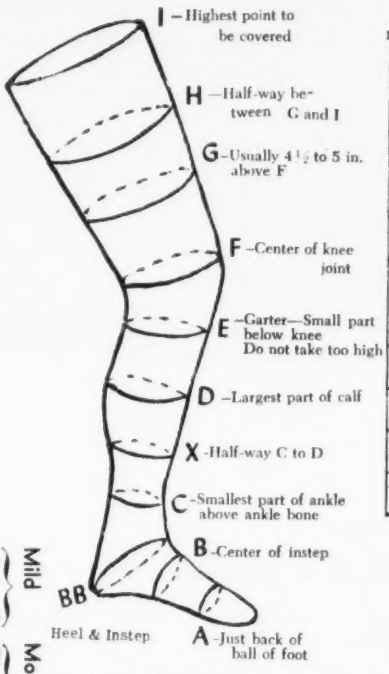
Arm Support	$ 8.00 ea.
Additional supports, same size	7.00 "
Underknee hose, from A to E	8.00 "
Additional supports, same size	7.00 "
Full thigh hose, from A to I	12.00 "
Additional supports, same size	11.00 "
Waist high garments	28.00 "
Additional supports, same size	26.00 "

The following information is necessary for the proper degree of compression in the support.

30 mm Hg—To assist fluid dynamics (prophylaxis) } Mild
30 mm Hg—Post Phlebitis Syndrome }

40 mm Hg—Varicose Veins (simple) } Moderate
40 mm Hg—Chronic Venous Insufficiency }

40 mm Hg—Lymphedema—1 + } Severe
50 mm Hg—Lymphedema—2 + and higher }


I—Highest point to be covered
H—Half-way between G and I
G—Usually 4½ to 5 in. above F
F—Center of knee joint
E—Garter—Small part below knee Do not take too high
D—Largest part of calf
X—Half-way C to D
C—Smallest part of ankle above ankle bone
B—Center of instep
BB
Heel & Instep
A—Just back of ball of foot

CIRCUM. RIGHT	CIRCUM. LEFT	LENGTHS
I		Knee (F) to I
H		
G		Knee (F) to H
F		Knee (F) to G
E		
D		Floor to Knee (F)
X		Floor to E
C		
BB		Floor to D
B		Floor to X
A		

We allow for Compression—Measurements should be taken snug, but not tight, and in the morning before the limb becomes swollen.

Circumference measurements should be taken at points marked by letter on illustration.

Lengths should be taken on INNER SIDE of leg.

THE F. A. RITTER CO.

Manufacturers of Fine Knitted Elastic Fabrics and Surgical Orthopedic Appliances Since 1919

4624 WOODWARD AVE. DETROIT 1, MICHIGAN

We also knit Custom made one-way and two-way stretch stockings . . . Service weight and fine weight . . . of linen, cotton, nylon, durene, silk . . . in natural, sun tan, pink or white . . . also fine rubber one-way stretch stockings equipped with two-way stretch knee and top welt.

don't just hide
housewife's eczema!
heal it with...

POLYSORB® HYDRATE

rational therapy for hand eczemas

Neither a barrier cream nor an oil, POLYSORB HYDRATE works naturally to protect and heal inflamed hands. By emulating skin's own water-in-oil emulsion, it protects hands from detergents and other irritants. At the same time, POLYSORB HYDRATE permits a dynamic interchange of fluid that prevents maceration or excessive dryness and aids rapid and complete healing of inflamed dry skin eczemas.

Available in 50-gram tubes, POLYSORB HYDRATE is a water-hydrated, specially processed, balanced emulsion of sorbitan [illegible] and trace metabolites.

FOUGERA E. FOUGERA & COMPANY, INC.
New York 13, N. Y.

Of interest to you

and your patients

THE MENACE OF ALLERGIES

WHAT WE KNOW ABOUT ALLERGY
by Louis Tuft, 12 pages, 15 cents

HOUSE DUST ALLERGY
by Karl D. Figley, 8 pages, 15 cents

FOOD ALLERGY
by Samuel M. Feinberg, M.D., 6 pages, 10 cents

SKIN ALLERGY
by Samuel M. Feinberg, M.D., 6 pages, 10 cents

ASTHMA AND HAY FEVER
by Samuel M. Feinberg, M.D., 6 pages, 10 cents

RAGWEED AND HAY FEVER
by Oren C. Durham, 2 pages, 5 cents

AMERICAN MEDICAL ASSOCIATION
535 NORTH DEARBORN STREET • CHICAGO 10 • ILLINOIS

Announcing

TRIDENOL®

Soothing Olive Oil Bath Additive

Permits Pruritus Patients to Bathe in Comfort

TRIDENOL is a thoroughly effective, clinically desirable, mildly scented, new, soothing, preparation for addition to the bath. For the relief of patients who suffer from dry skin, and who experience itching and burning after bathing.

TRIDENOL, when added to the bath, leaves a thin film of pure olive oil on the skin. This acts as a soothing agent for irritated, itching and sensitive skin, and prevents loss of moisture.

TRIDENOL is highly purified imported olive oil, made dispersible in hard or soft water by means of a non-irritating, non-ionic, surfactant, octylphenoxyethanol.

Supplied: 8 oz. plastic bottles.

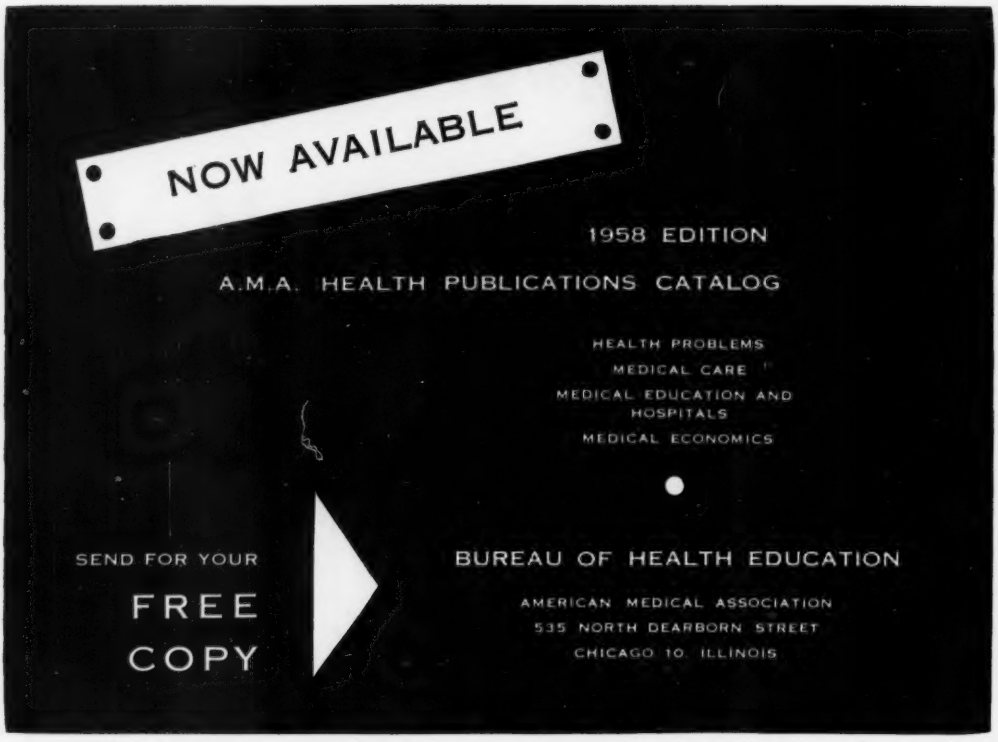
Professional samples available on request.

TRIDENOL

Old Alchemic Sign For Olive Oil and Neptune King of the Sea

Spirt & Co., Inc.
WATERBURY, CONNECTICUT

REFERENCE:
Knox, J. M., Everett, M. A., and Curtis, A. C.: New Uses For Surface-Active Agents. A.M.A. Arch. Derm. 74:699-706 (Dec. 1956)



YOUR GUIDE TO MEDICAL LITERATURE

QUARTERLY CUMULATIVE INDEX MEDICUS

Divided into sections, one devoted to books and the other to periodical literature, the QUARTERLY CUMULATIVE INDEX MEDICUS contains, in its major part, a compilation of periodical references by author and subject arranged in one alphabet for easy use. The exact bibliographic reference is given under the author with the title in the original language, while titles under subject headings are all in English. The index also includes a listing of journals, addresses and publishers.

The QUARTERLY CUMULATIVE INDEX MEDICUS appears twice a year; volumes are cloth bound and cover periodicals received within the six months indicated. These volumes are a convenient and inclusive reference for current medical literature. Invaluable for practitioners, specialists, teachers, editors, writers, investigators, students and libraries.

Subscription Price $25.00 Per Year
Canadian and Foreign $27.00 Per Year

AMERICAN MEDICAL ASSOCIATION • 535 N. DEARBORN ST. • CHICAGO 10, ILL.

No longer *itched*

bothered or

bewildered

Pruritus is relieved rapidly and erythema and lichenification of the skin are reduced within a short period after initial application of NEO-CORT-DOME. Secondary infection is controlled and the normal pH of the skin and external auditory canal is restored and maintained with NEO-CORT-DOME.

FOR INFECTIOUS DERMATOSES AND OTITIS EXTERNA

NEO-CORT-DOME™

CREME AND LOTION pH 4.6

Hydrocortisone-Neomycin-In Aluminum Acetate Vehicle

DOME

ACID MANTLE-HYDROCORTISONE-NEOMYCIN

INCORPORATED IN EXCLUSIVE ACID MANTLE VEHICLE

Note: Lotion is especially effective in hairy areas and in tissue folds. *Supply:* ½% or 1% hydrocortisone, with 5 mg. per gm. Neomycin Sulfate in ½ oz., 1 oz., 4 oz. squeeze bottles. (½ oz. size has special soft plastic tip for easy application into external ear in otitis externa). *Sample* and literature available on request.

DOME CHEMICALS INC.
125 West End Avenue, New York 23
665 N. Robertson Blvd., Los Angeles 46
In Canada: 2675 Bates Road, Montreal

A. M. A.
AMERICAN JOURNAL
OF
DISEASES OF
CHILDREN

integrate your knowledge—
subscribe to

A. M. A. Archives of PATHOLOGY

A. M. A. Archives of INTERNAL MEDICINE

A. M. A. Archives of OPHTHALMOLOGY

A. M. A. Archives of OTOLARYNGOLOGY

For a more complete reference shelf, we recommend these related journals. The variety of fields covered are especially appealing to the general practitioner with special interests. Each issue is important to your practice. Begin your subscriptions TODAY.

Department (D. C.)
AMERICAN MEDICAL ASSOCIATION
535 N. Dearborn St.
Chicago 10, Ill.

Begin my subscription(s) NOW, for:

A. M. A. .....
NAME .....
STREET .....
CITY ....STATE .....

integrate your knowledge by reading these related specialty journals . . .

A. M. A. Archives of INDUSTRIAL HEALTH

A. M. A. Archives of INTERNAL MEDICINE

A. M. A. Archives of DERMATOLOGY

Designed to save you hours of reading time through visual presentations . . . to provide you with timely tips every month . . . to place useful information at your finger tips, leaving less information on your reference shelf.

Write for subscriptions to:
AMERICAN MEDICAL ASSOCIATION
535 North Dearborn Street
Chicago 10, Ill.
Dept. (PATH.)

Anyone can have a
DRY SKIN PROBLEM

—and almost everyone can find relief with Allercreme Hypo-allergenic Lubricants. Whether your patients are troubled with moderately dry skin or extremely dry skin—whether they can or cannot tolerate lanolin or perfume—whether they prefer soothing lotions and creams or a bath oil—there is an Allercreme Hypo-allergenic Lubricant for your selection.

Allercreme Skin Lotion—scented or unscented—is an oil-in-water emulsion containing lanolin derivatives for lubrication of moderately dry skin. *Special Formula* Skin Lotion—scented or unscented—is a companion lanolin-free lotion for similar use.

Allercreme Body Lotion—scented or unscented—is a heavier oil-in-water emulsion containing lanolin derivatives for the lubrication of extremely dry skin. *Special Formula* Body Lotion—scented or unscented—is a companion lanolin-free lotion for similar use.

Allercreme Lubricating Cream—scented or unscented—is a semi-solid oil-in-water emulsion containing lanolin derivatives for the lubrication of the face, throat and pressure problem areas. *Special Formula* Lubricating Cream—scented or unscented—is a companion lanolin-free night cream for similar use.

Allercreme Bath Oil—lanolin free—diffuses instantly throughout bath water into countless tiny droplets of soothing oil which lubricate the entire body while bathing. Pleasantly scented with the exclusive Allercreme Hypo-allergenic Perfume—a synthetic fragrance containing neither animal extracts nor flower oils.

For additional information and sources of supply, write

Allercreme
HYPO-ALLERGENIC
COSMETICS

Division of Texas Pharmacal Company
San Antonio

growing clinical testimony

1956

(1) Miller, E. W., Jr.: New York J. Med. *56*:1446, 1956.

1957

(2) Garnes, A. L., and Barnard, R. D.: Angiology *8*:13, 1957. (3) Morrison, J. E., and Casali, J. L.: Am. J. Surg. *93*:446, 1957. (4) Miller, J. M.; Godfrey, G. C.; Ginsberg, M., and Papastrat, C. J.: Postgrad. Med. *22*:609, 1957.

1958

(5) Katz, R. I.; Reese, J. W., and Byrne, J. J.: Am. J. Surg. *95*:102, 1958. (6) Carpenter, E. B.: Virginia M. Month. *85*:22, 1958. (7) Wood, O. H.: Maryland M. J. *7*:265, 1958. (8) Burke, J. F., and Golden, T.: Am. J. Surg. *95*:828, 1958. (9) Miller, J. M.: Surgery *43*:939, 1958. (10) Carter, C. H., and Maley, M. C.: M. Times, in press.

on a unique debriding-healing agent

Panafil® OINTMENT

The increasing body of clinical evidence proves PANAFIL Ointment singularly effective in the treatment of chronic and infected wounds and ulcers.

All investigators[1-10] agree that PANAFIL produces and maintains a clean wound base and encourages normal healing.

The rapid, clean healing observed with PANAFIL therapy results from a unique combination of ingredients:

- **Papain,** a proteolytic enzyme—digests necrotic tissue and liquefies exudate without harm to healthy tissue—tends to eliminate local infection by removing the bacteria-supporting substrate.
- **Urea,** a protein-solvent—augments the debriding action of papain by exposing protein substrates to complete proteolysis.
- **Chlorophyll Derivatives** (water soluble)—control inflammation by protecting viable tissue from the effects of protein breakdown products—encourage normal healing, reduce necessity for skin grafting.

PACKAGING: Available *on prescription only* in 1-oz. and 4-oz. tubes.

Panafil for local treatment of wounds and ulcers

Rystan company · MOUNT VERNON, NEW YORK

30958

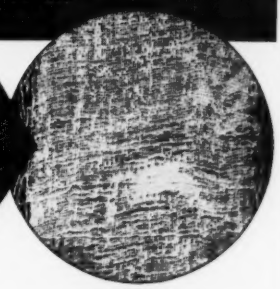
THE BEST IMPROVEMENT YET IN *UNNA'S BOOT*

NEW 4" x 10 YD.

Non-Ravelling

DOME-PASTE® BANDAGE

DOME

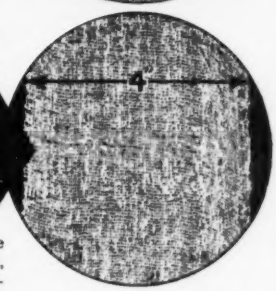


THE OLD

Frayed edges, uneven impregnation, difficult to apply.

•

Thread-locked edges, firmly woven; medicament spreads uniformly, easy to apply.



THE NEW

The new Dome-Paste bandage is flesh colored, 4" x 10 yd. gauze bandage... impregnated with glycerine, zinc oxide, gelatine paste.

RECOMMENDED

for leg ulcers resulting from thrombophlebitis (particularly the post partum and post-operative kinds), stasis edema and chronic venous insufficiency associated with varicose veins, and varicose eczema, lymphatic edema and thrombophlebitis of the superficial saphenous vessels.

AVAILABLE

Individually wrapped in sealed polyethylene bags, inserted in metal cans to insure freshness.

DOME
CHEMICALS INC.
109 WEST 64th ST. NEW YORK 23, N.Y.

AN *Ethix* FORMULA

UNSCENTED

SHAMPOO

Myristic and lauric acids saponified with polyamine alkali to a low pH(8), with neutralized polycarboxylic acid, enriched with lanolin esters, given extraordinary solvency with propylene glycol.

Vegetable or mineral tars may be added in desired percentage.

Removes ointments and medications gently but thoroughly.

High foaming, extremely economical in use.

Tolerated by scalps which shed epithelium from overstrong detergents.

RETAIL PRICE
$1.50
BOTTLE
6 OZ.

ETHIX CORPORATION
P. O. Box 115, Inwood 96, L. I., N. Y.
Send 1 oz. sample bottles of ETHIX FORMULA Shampoo to:

..... M.D.

.....

.....

9 SPECIALTY JOURNALS

PUBLISHED MONTHLY

BY THE AMERICAN MEDICAL ASSOCIATION

NEUROLOGY AND PSYCHIATRY

DISEASES OF CHILDREN

INTERNAL MEDICINE

INDUSTRIAL HEALTH

OTOLARYNGOLOGY

OPHTHALMOLOGY

DERMATOLOGY

PATHOLOGY

SURGERY

each journal offers
the latest medical findings by
outstanding authorities in
its special field . . .
of value not only
to the specialist but
to the general practitioner as well

to order your subscription to one of the A.M.A.'s
specialty journals use the form below

AMERICAN MEDICAL ASSOCIATION
535 North Dearborn • Chicago 10

Please enter my subscription to the specialty journal checked at right.
Remittance for ☐ one year ☐ two years is enclosed.
Start my subscription with the next Issue.

NAME_____

ADDRESS_____

CITY_____ ZONE____ STATE_____

	U.S.A. & Possessions APO's	Canada	Outside U.S.A. & Possessions
☐ A.M.A. Arch. Neurology and Psychiatry	$14.00	$14.50	$15.50
☐ A.M.A. Arch. Dermatology	12.00	12.50	13.50
☐ A.M.A. Arch. Industrial Health	10.00	10.50	11.50
☐ A.M.A. Arch. Internal Medicine	10.00	10.50	11.50
☐ A.M.A. Jrl. Diseases of Children	12.00	12.50	13.50
☐ A.M.A. Arch. Surgery	14.00	14.50	15.50
☐ A.M.A. Arch. Pathology	10.00	10.50	11.50
☐ A.M.A. Arch. Ophthalmology	12.00	12.50	13.50
☐ A.M.A. Arch. Otolaryngology	14.00	14.50	15.50

A. M. A.
AMERICAN JOURNAL
OF
DISEASES OF
CHILDREN

integrate your knowledge—
subscribe to

↓

A. M. A. Archives of
PATHOLOGY

↓

A. M. A. Archives of
INTERNAL MEDICINE

↓

A. M. A. Archives of
OPHTHALMOLOGY

↓

A. M. A. Archives of
OTOLARYNGOLOGY

For a more complete reference shelf, we recommend these related journals. The variety of fields covered are especially appealing to the general practitioner with special interests. Each issue is important to your practice. Begin your subscriptions TODAY.

Department (D. C.)
AMERICAN MEDICAL ASSOCIATION
535 N. Dearborn St.
Chicago 10, Ill.

Begin my subscription(s) NOW, for:

A. M. A. .....

NAME .....

STREET .....

CITY .....STATE .....

℞ For Household Hand Dermatitis

KNIT COTTON LINED

Bluettes®

Neoprene Rubber Gloves

Bluettes' knit cotton lining is permanently bonded to the liquidproof neoprene exterior, eliminating separate glove and liners. Regular hand or machine washing will not affect lining, bond or neoprene.

Patch Test Kits

contain 1 centimeter diameter discs of Pioneer glove materials.

Mail Coupon For Patch Test Kits

The PIONEER Rubber Company
106 Tiffin Road, Willard, Ohio

Please send me:

☐ Patch Test Kit #7 — Household Glove Patch Test discs.

☐ Patch Test Kit #8 — Industrial Glove Patch Test discs.

NAME _____

ADDRESS _____

CITY _____ Zone ___ State _____

SEBASUM*

*TRADEMARK

SEBASUM is effective as an aid in treating Acne. A pleasantly scented solution containing polysorbate 80, U.S.P., alcohol and acetone, SEBASUM removes excess oils from the skin, penetrating the sebaceous follicles through the action of its emulsifying and cleansing agents. Widely used in treating Acne and other seborrheic conditions, SEBASUM prepares the skin for supplemental therapy, if indicated. SEBASUM is well tolerated. It is pleasant and comforting to the patient. SEBASUM evaporates readily and will not stain or leave greasy residuals.

SEBASUM is packaged in attractive four fluidounce and pint bottles.

Ask your pharmacist to stock SEBASUM for your prescriptions.

Additional literature and samples sent on request.

SUMMERS LABORATORIES
INCORPORATED
AMBLER, PENNSYLVANIA

"Doctor, will you tell me..."

What are the symptoms?
How shall I treat it?
What causes it?

For practical information about communicable disease, have your patients read:

SCARLET FEVER
8 pages, 15 cents

IMMUNIZATION
by Ruth A. Thomas, 8 pages, 15 cents

WHOOPING COUGH
by Constance Frick, 4 pages, 10 cents

PNEUMONIA'S WATERLOO?
by William W. Bolton, 12 pages, 15 cents

WE CAN PREVENT DIPHTHERIA
by P. S. Rhoads, 8 pages, 15 cents

AMERICAN MEDICAL ASSOCIATION • 535 NORTH DEARBORN • CHICAGO 10

THE FUNGUS DIAGNOSTIC SERVICES

- **Direct microscopic reports by return mail.**
- **Simply mail in skin scrapings, blister tops, hair, or nail clippings folded into a slip of paper.**
- **Send exudates in a sterile tube.**
- **Identification of your own cultures.**
- **Inquiries invited.**

H. C. GOLDBERG, M.D., Diplomate Amer. Board of Dermatology
M. G. GOLDBERG, B.S., Mycologist, 7 Watchung Avenue, Plainfield, N. J., PL 6-7645

embarrassment is often the reason patients seek acne treatment

Most acne patients are deeply embarrassed by their unsightly lesions. A good acne preparation, therefore, should be cosmetic as well as curative.

'Acnomel' Cream and Cake achieve both aims of acne therapy. 'Acnomel' in either form conceals as it heals. The flesh-tinted base masks acne lesions and reduces embarrassment. The effective combination of sulfur, resorcinol and hexachlorophene acts to heal these lesions.

Used in combination, 'Acnomel' Cream and Cake provide 24-hour acne therapy. The Cream is excellent for use at home, morning or night, while the Cake, in its handy compact, is particularly convenient for touch-up medication away from home.

Acnomel* Cream and Cake

conceals as it heals

SKF SMITH KLINE & FRENCH LABORATORIES

*T.M. Reg. U.S. Pat. Off.

five

reasons for using

AVEENO® OINTMENT

as a base for your prescriptions

- **Absorbs skin exudates**
- **Soft creamy texture**
- **Washes off easily**
- **More soothing (because it contains Aveeno Colloidal Oatmeal)**
- **Anti-bacterial**

AVEENO® OINTMENT is compatible with all medicaments that may be added to Lassar's Paste. Typical compatibilities are:

Salicylic Acid	Phenol
Sulfur	Ichthammol
Ammoniated Mercury	Coal Tar
Resorcinol	Hydrocortisone

Active Ingredients: Aveeno® Colloidal Oatmeal, zinc oxide and 0.5% hexachlorophene in an emollient base.

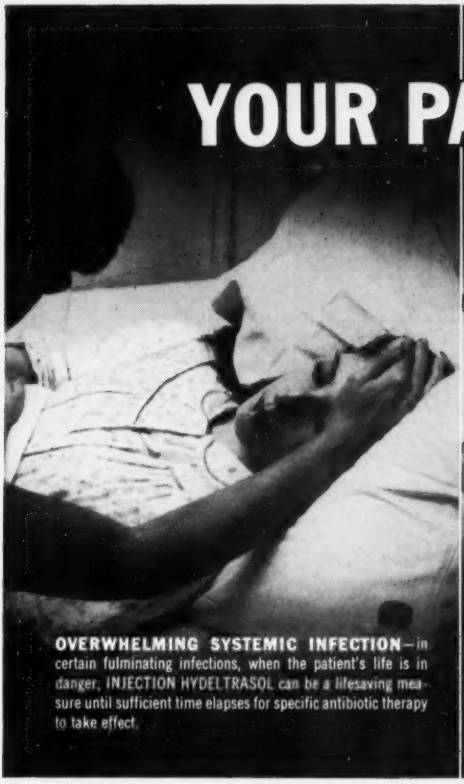
AVEENO® OINTMENT
Lassar's Paste—MODERNIZED

AVEENO OINTMENT is now available in a 4 oz. economy size tube as well as the 1 oz. tube.

Samples available on request

AVEENO **AVEENO CORPORATION** • New York 19, N. Y.

YOUR PATIENT?



OVERWHELMING SYSTEMIC INFECTION—in certain fulminating infections, when the patient's life is in danger, INJECTION HYDELTRASOL can be a lifesaving measure until sufficient time elapses for specific antibiotic therapy to take effect.

DISABLED ARTHRITIC—INJECTION HYDELTRASOL provides strikingly prompt relief from pain, discomfort and disability—may be administered with HYDELTRA-T.B.A.® for prompt onset of action and prolonged duration of relief [CYCLAINE® (Hexylcaine Hydrochloride) may be used initially to locate trigger points before injection].

In your bag...
ready for use...
IMMEDIATELY!

THE FIRST READY-TO-USE,
SOLUBLE,
ALL-PURPOSE
PARENTERAL STEROID

INJECTION HYDELTRASOL®

(Prednisolone 21-Phosphate)

ADVANTAGES:

1. Immediately effective—dramatic response in minutes
2. Ready for use—needs no reconstitution or refrigeration
3. In solution—flows readily through a small-bore needle

SUPPLIED: In 2-cc. and 5-cc. vials, each cc. containing 20 mg. of prednisolone 21-phosphate as the di-sodium salt.

Hydeltrasol is a trademark of Merck & Co., Inc.

MERCK SHARP & DOHME DIVISION OF MERCK & CO., INC., Philadelphia 1, Pa. MSD

QUARTERLY CUMULATIVE INDEX MEDICUS

YOUR GUIDE TO MEDICAL LITERATURE

Divided into sections, one devoted to books and the other to periodical literature, the QUARTERLY CUMULATIVE INDEX MEDICUS contains a list of current publications alphabetized as to authors and subjects. The exact bibliographic reference is given under the author with titles in the original language, while titles under subjects are all in English. The index also includes a listing of journals, addresses and publishers.

LISTED BY AUTHORS AND SUBJECTS

The QUARTERLY CUMULATIVE INDEX MEDICUS appears twice a year; volumes are cloth bound and cover periodicals for six months as indicated on the publication. These two volumes will be a convenient and inclusive reference for current medical literature. Invaluable for practitioners, specialists, teachers, editors, writers, investigators, students and libraries.

SUBSCRIPTION PRICE $25.00 PER YEAR
CANADIAN AND FOREIGN $27.00 PER YEAR

AMERICAN MEDICAL ASSOCIATION
535 NORTH DEARBORN STREET
CHICAGO 10, ILLINOIS

normal protective cover

Normal skin has an acid pH range between 4 and 6

Samples and literature on request

Supply:
ACID MANTLE Creme: 1 oz. tubes, 4 oz. & 16 oz. jars.
ACID MANTLE Lotion: 1 oz. and 4 oz. squeeze bottles, 1 pint bottles.

ACID MANTLE®

CREME or LOTION pH 4.2

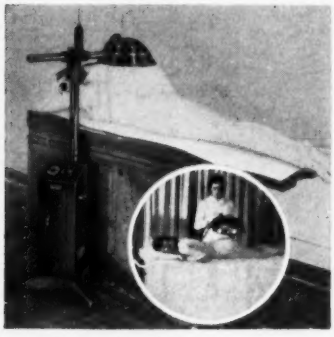
In housewives' eczema and industrial dermatitis, promptly restores and maintains the normal protective acidity of the skin. Active ingredient is aluminum acetate in specially formulated bases.

"The importance of a measure designed to return the pH of the skin quickly to its normal values after exposure to soap and alkalies is amply borne out..."

—Gross, P., et al.: A. M. A. Arch. Dermat. & Syph. 70:94,1954.

DOME *Chemicals Inc.*
109 WEST 64 ST., NEW YORK 23, N.Y.
665 N. Robertson Blvd., Los Angeles, Calif.
In Canada: 2765 Bates Rd., Montreal, P.Q.

THE ORIGINAL FISCHERQUARTZ



Model No. 88

A MUST IN DERMATOLOGY
OVER 48,000 MANUFACTURED SINCE 1928
HIGH POWERED GERMICIDAL ULTRAVIOLET
FOR LOCAL SKIN THERAPY AND FOR
CONSTITUTIONAL EFFECTS

No. 595
Localizer

R. A. FISCHER & CO.

517 Commercial St., Glendale 3, Calif.

SEND MEDICAL REPRINTS TO:

Name .....

Address .....

City..... Zone..... State.....

(no obligation)

fischer

FISCHERTHERM — FISCHERSINE — FISCHERQUARTZ — PEDASINE — FISCHER ULTRA SOUND
GALVANIC AND HIGH FREQUENCY EPILATORS

*TELES

Torch (available on prescription in 4 oz. bottles)

Really new, prompt and effective therapeutic agent in control of seborrheic dermatitis, itchy scalp and dandruff.

TELES • is a milk-white, unscented shampoo
TELES • may be employed at weekly intervals or less frequently
TELES • does not stain hair of any color
TELES • does not stimulate oiliness in the scalp
TELES • complete directions for use on each 4 oz. bottle

Samples and literature on request

Reference: Gross E. R. and Wright C. S., A. M. A. Archives of Dermatology, 78:92, July, 1958

TORCH LABORATORIES, INC.

110 Chestnut Street • Philadelphia 6 • Pa. *Tellurium Dioxide Suspension, Torch

---

Pleasingly and efficiently
serving patient and physician
during all seasons

SUPERFATTED

BASIS® SOAP

For dry sensitive skin

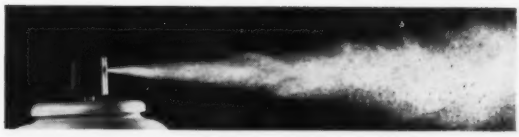
Available at Prescription Pharmacies

DUKE LABORATORIES, INC.
SOUTH NORWALK, CONN., U. S. A.

Mfrs. of Aquaphor®—Elastoplast®

in a form to fit

every antibiotic

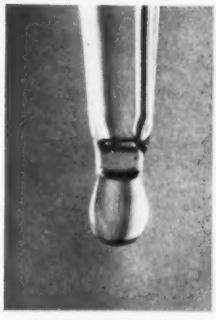
need  ...

ACHROMYCIN*

ACHROMYCIN Tetracycline

ACHROMYCIN V Tetracycline with Citric Acid Lederle

a most widely used and useful... antibiotic



ACHROMYCIN V: Capsules • Pediatric Drops • Syrup

ACHROMYCIN: Capsules • Ear Solution 0.5% • Intramuscular • Intravenous • Nasal Suspension with Hydrocortisone and Phenylphrine Ointment 3% • Ointment 3% with Hydrocortisone 2% • Ophthalmic Oil Suspension 1% • Ophthalmic Ointment 1% • Ophthalmic Ointment 1% with Hydrocortisone 1.5% • Ophthalmic Powder (Sterilized) • Oral Suspension • Pediatric Drops • Soluble Tablets SPERSOIDS® Dispersible Powder • Surgical Powder (Sterilized) • Syrup • Tablets • Topical Spray

*Reg. U. S. Pat. Off.

LEDERLE LABORATORIES, a Division of **AMERICAN CYANAMID COMPANY,** Pearl River, New York

Lederle

197/

TO PROTECT SKIN

AGAINST A WIDE RANGE OF IRRITANTS

- *in industry*
- *in the home*

Silicote provides an important advance in protecting skin from dry and aqueous irritants—prophylactically to prevent skin maceration, and therapeutically to exclude water, soap, and other substances from dermatoses that may be aggravated by them.

Clinical tests show that Silicote provides excellent protection against soap and water and soluble cutting oils.[1]

The protective property of Silicote is purely mechanical. Protective efficiency is necessarily determined by the nature and frequency of exposure. Frequency of application should be adjusted to provide adequate protection with minimum dosage.

SUGGESTED DOSAGE: Cleanse area thoroughly with soap and water. Apply thin film as required and rub in well. If skin is exposed constantly to irritant, apply every 2-4 hours, or as needed to provide protection. It is not necessary to remove original coat before applying subsequent coats. Any objectionable greasiness may be removed by wiping with a dry cloth, or washing gently with soap and water.

CONTRAINDICATIONS: Do not use on weeping or infected areas.

In Housewife's Eczema
Industrial Dermatoses
Chapping—Chafing
Intertrigo
Diaper Rash
Chronic Dermatoses
Aggravated by Soap
and Water

SILICOTE CONTAINS
30% dimethicone (silicone) in a specially prepared petrolatum base. Contains no water-soluble ingredients.

Send for samples and literature

1. Shaw, J. M., and Crowe, F. W.: Skin Protective Ointments. Arch. Dermat. & Syph. 71: 379, 1955.

SILICOTE
SILICONE OINTMENT

ARNAR-STONE LABORATORIES, INC. **MT. PROSPECT, ILLINOIS**

In Canada: Brent Laboratories, Ltd. Toronto

TO TREAT

ITCHY, SCALY SCALP

WHICH TENDS TO DRYNESS

sebulex®

ANTISEBORRHEIC SHAMPOO

WESTWOOD PHARMACEUTICALS, Buffalo 13, New York

sebulex®

a therapeutic shampoo for the treatment of itchy, scaly scalp which tends to dryness

Stops itching, removes loose dandruff and crusty, matted layers of scales from the scalp through the effective cleansing, penetrating and antiseborrheic actions of *Sebulytic*®, a combination of anionic surface-active cleansers and wetting agents. The antiseborrheic qualities of Sebulytic are further enhanced with the addition of sulfur and salicylic acid. Hexachlorophene provides antibacterial action.

Prevents excessive drying of the scalp through the action of *Kerohydric*™, a crystal-clear, dewaxed fraction derived from lanolin. Kerohydric also leaves the hair soft and more manageable after shampooing.

Sebulex is cosmetically elegant. Sebulex meets the up-to-date "cosmetic" requirements for a therapeutic shampoo. It has a smooth, lotion-like texture, an appealing pastel green color, delightful fragrance and produces an abundant lather. Patients like shampooing with Sebulex.

Sebulex does not contain any toxic metallic materials. Thus, it can be used for a prolonged period of time without danger of systemic toxic effects.

Sebulex contains a mixture of anionic surface-active cleansers and wetting agents (Sebulytic). These agents consist of sodium lauryl sulfoacetate, sodium alkyl aryl polyether sulfonate, and sodium dioctyl sulfosuccinate. Sebulex also contains Kerohydric, a crystal-clear, dewaxed fraction of lanolin; sulfur 2%, salicylic acid 2% and hexachlorophene 1%.

Available: In plastic bottles of 4 oz. *Write for samples.*

WESTWOOD PHARMACEUTICALS, Buffalo 13, New York

88% CURE RATE

in a wide variety of PYODERMAS

BACIMYCIN®

[BACITRACIN-NEOMYCIN] OINTMENT

a first choice for dual antibiotic therapy

In a recent study[1] of 53 patients with various types of pyodermas, the use of BACIMYCIN Ointment "... resulted in a cure rate of 88%...." Impetigo, infectious eczematoid dermatitis, atopic eczema, secondary infections superimposed on dermatitis venenata, and folliculitis were among the common skin infections that showed marked improvement with BACIMYCIN therapy.

BACIMYCIN rarely produces sensitization or primary irritation.

Supplied in ½ oz. tubes for prescriptions; in 100 gm. jars for hospital use; in ⅛ oz. tubes for ophthalmic use. Also supplied as BACIMYCIN with Hydrocortisone, ⅛ oz. tube with applicator tip.

Literature and samples on request.

1. Greenhouse, J. M., and Ryle, W. C.: A.M.A. Arch. Dermat. & Syph. 69:366 (March) 1954.

Walker **LABORATORIES, INC.** MOUNT VERNON, NEW YORK

CULTURE MEDIA AVAILABLE

Mycosel Agar

Sabouraud's Dextrose Agar

Sabouraud's Maltose Agar

Corn Meal Agar

Potato Dextrose Agar

Sabouraud's Dextrose with Penicillin

Sabouraud's Dextrose with Streptomycin

Chlamydospore Agar

Littman's Oxgall Agar

"It is considerably cheaper to use these bottles once and discard them than to pay the labor cost of reconditioning an equal number of test tubes."

...*Practical Medical Mycology*
By J. Walter Wilson, M.D.
and Orda A. Plunkett, Ph.D.
Arch D & S 59:414, April 1949

A PREFERRED METHOD for the CULTURE of FUNGI as an OFFICE PROCEDURE

WRITE FOR INFORMATIVE LITERATURE

DERM MEDICAL Sterile Glass Containers holding Sabouraud's Dextrose Agar offer a simple, accurate method for the culture of fungi pathogenic to man. When indicated for diagnosis and study of mycotic diseases, can be used as a routine office procedure. For institutional use, this method has proved both efficient and economical.

Derm Medical

Manufacturers of Culture Media in Sterile Containers

DM 3-4

DEPT. "D", P.O. BOX 78595 • WEST ADAMS STATION • LOS ANGELES 16, CALIF.